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CARDIAC AND PULMONARY EVALUATION IN ELDERLY PATIENTS BEFORE ELECTIVE SURGICAL OPERATIONS

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The possibility of identifying patients who are liable to suffer complications after surgery was investigated in 482 patients with respect to three tests: the electrocardiogram, the ballistocardiogram, and a test designed to measure restrictive and/or obstructive factors affecting ventilation. There were 212 patients between 60 and 90 years of age, and in this group the incidence of unfavorable test results as well as postoperative complications was higher than in the younger age groups. There was little correlation between electrocardiography and the subsequent course of the individual patient. Increase in postoperative complications is noticed in patients having abnormal ballistocardiograms and ventilation defects. The respiratory test was of value in enabling the surgeon to avoid major operations on the very few patients classed as prohibitive risks and to establish optimum operative conditions on patients with respiratory handicaps. The results of preoperative evaluation of the surgical patient by clinical impression without these tests proved to be of little value in geriatric patients.

THE INCREASE in life expectancy has resulted in a larger number of geriatric patients requiring surgery. The mortality and morbidity of the aged, after surgery, is higher than in younger patients. This usually is due to physiological derangements present preoperatively rather than directly to the surgery.[1] The value of proper preoperative evaluation, especially in the aged, need hardly be dwelt upon. The usual evaluation of operative risk is by clinical impression, based on the history, physical examination, and routine laboratory determinations. This is inadequate in geriatric patients, in whom the existence of some degree of degenerative changes such as arteriosclerosis and/or pulmonary emphysema is prevalent. There are many specific tests to evaluate cardiovascular and pulmonary function. However, most of them are too elaborate and time consuming to be practical for anesthesiologists. This paper is a presentation of our effort to perform an adequate, yet simple, evaluation of the patient preoperatively and an analysis of the relationship of postoperative complications to the existing abnormalities in cardiac or pulmonary physiology.

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Method

A day or two before the scheduled operation, the patient is seen in the preanesthesia clinic.[2] The history and physical examination are reviewed, and the following tests are performed:

1. A 12-lead electrocardiogram is taken, and the interpretation of the tracing is recorded on the preanesthesia chart. If there has been a previous electrocardiogram, a comparison is made to determine if any important changes necessitating further investigation have occurred.

2. A ballistocardiogram is obtained with use of a high-frequency Starr-type table. Results are recorded on a two-channel Sanborn direct writing recorder with simultaneous recording of the electrocardiogram on the other channel. The ballistocardiogram is then graded according to the degree of deviation from normal into the classes 0, 1, 2, 3, and 4 of Brown and associates.[3]

3. A one-breath ventilation test for vital capacity and a 0.5-second expiratory capacity test are performed with the use of the Gaensler-Collins timed vitalometer. The vital capacity is expressed as the percentage of the predicted vital capacity of the patient according to height and weight, with modification for the sedentary life of the aged. The 0.5-second expiratory capacity is expressed as the percentage of the actual measured vital capacity of the patient.[4] The results are classified as follows: (1) normal, indicated by a vital capacity of not less than 80% of the predicted value and a 0.5-second expiratory capacity of not less than 60% of the measured vital capacity; (2) restrictive lesion, indicated by a vital capacity below 80% of the predicted value and a 0.5-second expiratory capacity of 60% or more; (3) obstructive lesion, indicated by a vital capacity of 80% or more of the predicted value and a 0.5-second expiratory capacity below 60% of the actual vital capacity; and (4) combined lesion, indicated by a combination of the obstructive and restrictive lesion, with a vital capacity below 80%, and a 0.5-second expiration capacity below 60%.

In order to determine whether any benefit is to be gained from these physiological evaluations, the usual operative risk rating is done by the anesthesiologist administering the anesthesia, without previous knowledge of the result of these tests.

Four hundred eight-two patients were followed through the postoperative period. Of these patients, 92 had minor operations; 82, major head and neck operations; 50, radical mastectomy and superficial node dissection; 32, exploratory thoracotomy; 23, lobectomy, pneumonectomy, and esophagectomy; 47, operation on stomach, duodenum, liver, gallbladder or duct, pancreas, spleen, and small intestine; 109, pelvic operation and lower abdominal operation; 56, radical pelvic operation; 4, interscapular amputation or hemipelvectomy; 12, adrenalectomy; 1, kidney operation; 1, hypophysectomy; and 1, induction of anesthesia without operation. This gives a total of 516 procedures.

The complications, within two weeks of operation, excluding those complications directly resulting from surgery, such as massive hemorrhage, were graded according to severity as none, minor, major, and death. Among the minor difficulties were transient moderate hypotensive episodes, arrhythmias, and respiratory disturbances which required no treatment or responded promptly to symptomatic treatment. Major difficulties included shock, arrhythmias requiring intensive treatment, congestive failure, pulmonary edema, prolonged hypotension, myocardial infarction, atelectasis, pneumonia, respiratory insufficiency, renal shutdown, and electrolyte imbalance.

For purposes of comparison, the patients were separated into three age groups: group 1, consisting of patients between 16 and 39 years of age; group

TABLE 1.—*Relation of Age to Morbidity and Mortality*

Difficulties	Age, Yr. 16-39	40-59	60-90	Total
None	39	180	152	371
Minor	5	26	23	54
Major	1	13	21	35
Death	1	5	16	22
Total	46	224	212	482

TABLE 2.—*Relation of Age to Abnormal Ballistocardiogram Patterns*

Ballistocardiogram Class No.	Age, Yr. 16-39	40-59	60-90	Total
0	27	32	7	66
1	17	71	22	110
2	1	62	67	130
3	1	48	80	129
4	0	11	36	47
Total	46	224	212	482

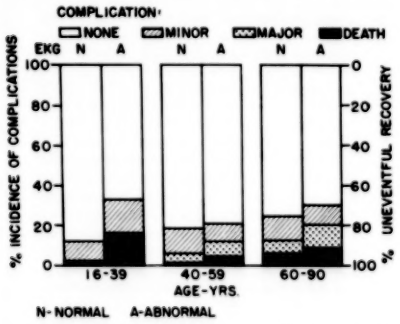

Fig. 1.—Correlation between electrocardiograms and incidence of postoperative complications.

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2, consisting of patients between 40 and 59 years of age; and group 3, consisting of patients 60 to 90 years of age. The morbidity and mortality among the different age groups and within each group were compared as to the different physiological disturbances diagnosed in the preanesthesia clinic.

Results

Four hundred eighty-two patients, ranging in age from 16 to 90, were evaluated in the preanesthesia clinic. There were 46 patients in group 1 (16 to 39 years of age), 224 patients in group 2 (40 to 59 years of age), and 212 patients in group 3 (60 to 90 years of age). The number of patients in group 1 is too small for analysis of correlation, but the other two groups are comparable.

The mortality and morbidity are shown in table 1. With advance in age, fewer patients have an uneventful operative and postoperative course. The incidence of serious complications and death is increased, while that of minor complications shows little variation.

Cardiovascular Evaluation.—The results of cardiovascular evaluation showed a definite trend with increasing age. In group 1 87% of the patients had a normal electrocardiogram. This decreased to 70% in group 2 and 44% in group 3. The electrocardiographic abnormalities observed in patients above 60 years of age were: nonspecific ST-segment changes, 19.3%; bundle branch block, 10.4%; ventricular premature contractions, 9%; left ventricular hypertrophy, 3.8%; auricular premature contractions, 3.3%; old myocardial infarction, 2.8%; auriculo-ventricular block, 2.8%; auricular fibrillation, 2.8%; and low voltage, 1.9%.

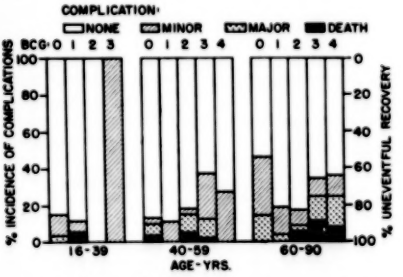

Fig. 2.—Relation between ballistocardiogram classifications and incidence of uneventful recoveries.

There is little definite pattern of correlation between the electrocardiogram and the incidence of postoperative complications (fig. 1). In the group over 60 years of age only two electrocardiographic abnormalities were associated with a high degree of postoperative complications. They were evidence of an old myocardial infarction and auricular premature contractions. In six patients with evidence of an old myocardial infarction, there was one death, two major and one minor complications. In four patients with auricular premature contractions there were one death and two major complications occurring postoperatively.

The ballistocardiogram also shows a tendency toward more abnormal patterns with increasing age (table 2). In group 1 classes 0 and 1 predominate,

TABLE 3.—*Relation of Age to Incidence of Lesions of the Respiratory Tract*

Respiratory Pattern	Age, Yr. 16-39	40-59	60-90	Total
Normal	14	73	28	115
Restrictive	2	17	28	47
Obstructive	7	39	40	86
Restrictive-obstructive	1	17	35	53
Total	24	146	131	301

in group 2 classes 1 and 2 occur more frequently, and in group 3 classes 2 and 3 are predominate. There were 46 patients in group 1, with 1 patient each in classes 2 and 3 and none in class 4. Therefore little significance could be attached to the incidence of complications during and after operation in relation to the classification of their ballistocardiograms. In the two groups above 40 years of age there is a decrease in the number of patients having an uneventful operative course and an increase in mortality and morbidity in those having classes 3 and 4 ballistocardiograms (fig. 2).

Respiratory Evaluation.—There is little difference in the incidence of the obstructive lesions of the respiratory tract in the three age groups. However, the number of restrictive and combined restrictive-obstructive lesions are increased with age (table 3). Only a small proportion of patients over 60 years of age have normal ventilation. Any type of ventilatory defect (obstructive, restrictive, or mixed) increases the incidence of postoperative complications in the older age group (fig. 3). The clinical impression that elderly patients with emphysema develop more complications postoperatively is confirmed by the greater incidence of complications in group 3 in patients with obstructive lesions.

Evaluation By Anesthesiologist.—The results of the comparison of the usual operative risk rating by the anesthesiologist to the complications occurring during operation and in the postoperative period is shown in figure 4. Good correlation is present in the two groups of patients below 60 years of age, but above this age the clinical impression of the anesthesiologist is of no value in predicting operative or postoperative complications. Patients rated as poor risks did as well as patients adjudged to be good risks.

Severity of Operations.—There was no increase in mortality and morbidity among elderly patients after minor or extensive superficial operations such

as radical mastectomy or groin dissection. During and after major surgery the mortality and morbidity is higher in the group over 60 years of age. This is especially pronounced among those who have undergone thoracic and upper abdominal operations.

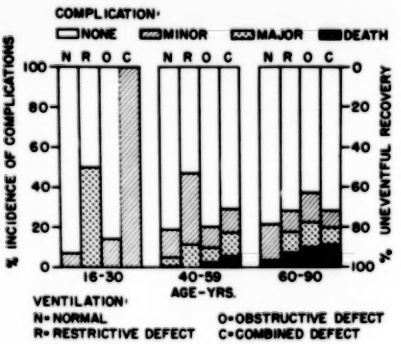

Fig. 3.—Relation of age to incidence of postoperative complications.

Comment

Much of the difficulty in the preoperative evaluation of geriatric patients is due to the presence of subclinical degenerative changes with impairment of the functional capacity or reserve of various organ systems. It would be desirable to be able to detect these changes and to have some indication of the extent of involvement, especially of the cardiovascular and pulmonary systems. The fact that the tests we use tend to give abnormal results in an increased proportion of the elderly patients is suggestive of some relationship to these degenerative changes.

The lack of correlation between the electrocardiogram and postoperative complications is not surprising since the electrocardiogram is not a measure of the functional capacity of the heart. The use of the electrocardiogram in heart disease detection for general screening purposes has been proposed from time to time. Internists differ in their opinion of its value, mainly because of its lack of precise correlation with the clinical symptoms of heart disease.[3] However, in the older age group the electrocardiogram may be an early clue to, or definite confirming evidence of, many abnormalities of the heart, such as diffuse myocardial disease, hyperirritability, conduction defects, and myocardial infarction.

Such specific information has been found most valuable in determining whether some preventive measure or further investigation is necessary in certain patients before the proposed surgical procedure. In addition, a preoperative electrocardiogram provides a good base line for comparison during the operation or in case of cardiac complications, postoperatively.

Levine, de Peyster, and Hannigan all found increased mortality and morbidity in surgical patients who had a healed myocardial infarction.[6] Both Levine[6a] and Finkbeiner and associates[7] found that chronic auricular fibrillation does not contribute to operative and postoperative complications, and Pfeiffer and LaDue[8] reported no increase in surgical mortality in patients with bundle-branch block. Our results confirm these observations.

The clinical application of the ballistocardiogram is not as well established as that of the electrocardiogram. In the young normal person it correlates quantitatively with the cardiac output as determined by Fick's principle. The ballistocardiogram is believed by most investigators to be primarily related to the strength of heart beat,[9] and there is a close association of the abnormal ballistocardiogram with coronary heart disease.[10] Various investigators have found it to be a sensitive indicator of the functional capacity of the heart in many divergent conditions such as paroxymal tachycardia, bundle-branch block, and angina pectoris.[11] It is especially informative when repeated record-

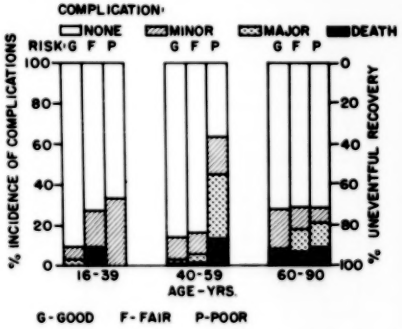

Fig. 4.—Comparison of anesthesiologist's risk rating and incidence of operative and postoperative complications.

ings of the same patient are taken at intervals and compared.[10] Some investigators have used it in conjunction with a standard exercise test.

We have found increased operative and postoperative morbidity and mortality in the patients with abnormal ballistocardiograms in this series. Although extreme caution should be exercised in

the interpretation of one single resting record, a nearly normal ballistocardiogram in the elderly patient justifies a more optimistic outlook, and a poor one in the younger serves as a warning signal.

Cooperative effort on the part of the patient is a necessity for any ventilation test, and ease in performance contributes greatly to accuracy of the results. The convenience in using a Gaensler-Collins vitalometer for ventilation tests has been shown by Miller, and Wu, and Johnson.[4]

Gaensler,[12] in 1951, used the timed vital capacity instead of the maximum breathing capacity for the detection of faulty expiratory flow rate. He found good correlation between the maximum breathing capacity and the first one-second portion of the expiratory vital capacity in the normal individuals. Miller and co-workers [13] demonstrated that the first 0.5-second portion of the expiratory vital capacity truly represents the maximum air flow; that it correlates well with the maximum breathing capacity in normal persons, and is superior to the maximum breathing capacity test in patients with abnormal ventilation because it is not affected by extrapulmonary factors.

The purpose of these ventilation tests is to enable us to avoid a major surgical procedure on the very few prohibitive respiratory risks and to establish optimum operative conditions for other patients by determining the necessity for preoperative respiratory therapy. Patients who have marked obstructive lesions should receive bronchodilators, expectorants, and, in some cases, antibiotics preoperatively.[4]

It is not the purpose of this presentation to go into the equally important aspects of renal function, blood volume, and electrolyte balance. Certainly, a fairly complete clinical chemistry and blood volume determination should be part of the routine preoperative examination of the geriatric patients. Abnormalities should be corrected accordingly before the surgery.

Summary and Conclusions

Simple tests including a 12-lead electrocardiogram, ballistocardiogram, and one-breath ventilation test for vital capacity and 0.5-second expiratory capacity were incorporated as part of a preanesthesia evaluation program for 482 geriatric patients. Correlation of the data with the subsequent operative and postoperative course indicated an increase in the incidence of postoperative complications in patients having abnormal ballistocardiograms and ventilatory defects. The usual method of evaluation of preoperative risk by clinical impression is of little value in geriatric patients. Definitive evidence of degenerative cardiopulmonary disease can often be elicited in the older age groups and serves as a guide for conduction of anesthesia and postoperative therapy.

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SEGMENTAL THROMBO-OBLITERATIVE DISEASE OF BRANCHES OF AORTIC ARCH

SUCCESSFUL SURGICAL TREATMENT

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Thrombo-obliterative disease of the branches of the aortic arch causes symptoms of ischemia in the head and upper extremities. In the two cases here described it was sharply delimited. In the first case its location was determined with the help of aortography; in the second, the physical findings with usual chest roentgenograms sufficed. In the first case two incisions in the neck were needed to settle the diagnosis and to permit thromboendarterectomy at the level of the carotid sinus; in addition, a right anterior thoracotomy in the second interspace was needed, and a bifurcated nylon tube was inserted to lead from the aorta past the obstructed brachiocephalic trunk to the right subclavian and common carotid arteries. In the second case an obstruction involving the left subclavian artery was removed by thromboendarterectomy. Normal pulsations reappeared in the arteries distal to the site of operation in each case. Both patients were relieved of symptoms and were able to return to work.

Segmental thrombo-obliterative disease of branches of the aortic arch is a term used to designate a clinical entity resulting from occlusion of one or more of the major branches arising from the aortic arch and characterized by manifestations of ischemic disturbances and absence of pulses in the head, neck, and upper extremities. Other terms which have been applied to this condition are the aortic arch syndrome, pulseless disease, reverse coarctation, Takayasu's disease, Martorell's syndrome, and thrombotic obliteration of the branches of the aortic arch. Although the condition was well described by Broadbent [1] in 1875, except for the report of Takayasu [2] in 1908, and subsequently of other Japanese ophthalmologists, little interest in the disease has been shown until recently, following particularly the report of Shimizu and Sano [3] in 1951. Their report with its eye-catching title, "pulseless disease," received wide recognition and undoubtedly gave much impetus to the greater awareness of the condition. Since then an increasing number of reports have appeared in both the American and the European literature, and in their recent thorough survey of these publications Kalmansohn and Kalmansohn [4] were able to collect 90 cases. Contrary to earlier indication that the disease was predominantly of Japanese origin, these reports would suggest that it has widespread geographical distribution and probably occurs more frequently than previously realized.

The etiology of this condition remains obscure, although various factors have been proposed as contributing to its causation, including syphilitic aortitis, nonspecific arteritis, atheromatosis, thromboangiitis obliterans, trauma, allergic reaction, and specific infections. These and other considerations of the etiology and pathogenesis recently have been thoroughly discussed by Ross and McKusick [5] and by Kalmansohn and Kalmansohn [4] in their extensive reviews of this subject. The disease tends to occur predominantly in young women; however, more recently, an increasing number of cases has been found in members of the male sex, and persons afflicted with it in the second through the seventh age decades have been encountered.

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Certain pathological features of the disease are noteworthy since, as will be indicated later, they have a significant bearing upon therapy. First, the pathological process appears to be fairly well localized, involving primarily the innominate, carotid, and subclavian arteries. The disease rarely extends beyond the course of these vessels in the neck, and proximally is limited to their origin from the aortic arch. Thus, the obliterative process seems to be quite segmental in character, with relatively normal arterial lumens proximally and distally. In this respect, the disease appears to be similar to the Leriche syndrome (thrombotic obliteration of the terminal abdominal aorta and bifurcation). Another noteworthy feature is that the histological nature of the lesion suggests periarteritis nodosa with intimal proliferation and thrombotic obliteration of the lumen, as well as fibroblastic proliferation of the media and adventitia.

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The clinical manifestations of the disease are rather protean, depending upon the nature and extent of the obliterative process and the adequacy of collateral circulation. In general, they may be classified into categories according to the parts of the human body—brain, eyes, face, and upper extremities—affected by the arterial insufficiency. The neurological disturbances resulting from cerebral ischemia vary considerably from relatively mild symptoms of headache, vertigo, and fainting attacks to more severe epileptiform convulsions and actual paralysis. Ocular disturbances range from photopsia to blindness. Skin and muscle atrophy, and even ulcerative lesions in the face, may occur as a result of inadequacy of circulation to these parts. Symptoms of arterial insufficiency in the upper extremities are usually mild, consisting mainly of weakness, increased fatigability, paresthesia, and occasionally claudication. Trophic changes are also mild and ischemic lesions are uncommon. The most striking findings in the upper extremities are absence of pulsations and of detectable blood pressure. Insidious in onset, the disease tends to assume a gradual course extending over a number of years with progressive increase in symptoms, cerebral ischemia being the most common cause of death.

Treatment of this disease by various medical means has been generally disappointing. Obviously, effective therapy must be directed toward restoration of normal blood flow, an objective which may best be approached by surgical means. As far as we have been able to determine from a review of the literature this has been attempted in only four cases. The first two cases were reported by Shimizu and Sano.[3] In one of the patients the procedure consisted of thrombectomy through the sacrificed external carotid artery, with denervation of the carotid sinus and removal of the carotid body; this operation was followed by "some relief." In the other patient, who had occlusion of the right subclavian and common carotid arteries, the procedure consisted of resection of the carotid bifurcation and the use of a venous homograft between the common and internal carotid arteries after sacrificing the external carotid artery. Although the syncopal attacks were relieved, an arteriogram "did not demonstrate much blood flow into the brain through this graft." In the third case, a modified endarterectomy of the left common carotid artery was performed by exposing the vessel in the neck and passing a probe proximally through the patent but contracted lumen into the aorta. A free flow of blood was obtained and pulsations in the artery restored, but the final result of this case was apparently not entirely satisfactory, since a subsequent operation became necessary. This second operation consisted of grafting the aorta of an infant between the aortic arch and the patent portion of the common carotid artery, and was followed by alleviation of dizziness, tinnitus, and convulsions.[5] In the fourth patient, who had occlusion of the innominate artery and partial obstruction of the left subclavian artery, thromboendarterectomy of the innominate artery was performed through a right anterior thoracotomy approach.[6] This resulted in improvement of the symptoms referable to the central nervous system and to the development of a "weak carotid pulse," but pulses in the right arm remained absent.

In the light of these observations, which reflect a paucity of surgical experience in this disease and indicate the generally equivocal results obtained, it seems desirable to report the following two cases in which the methods of surgical treatment employed were followed by complete restoration of normal circulation in the arterial bed of the occluded great vessels. Of added interest is the fact that they represent successful surgical treatment of claudication in the upper extremity and are the only recorded cases in which treatment was directed toward this symptom.

Report of Cases

Case 1.—A man 51 years old was admitted on Dec. 17, 1956, to the Houston Veterans Administration Hospital because of pain and weakness in the right upper extremity. Six months prior to admission, he had been forced to discontinue work as a painter because of claudication in the right forearm and arm. He had had no visual symptoms, syncopal attacks, or convulsions; the only symptoms indicating possible cerebral ischemia were lassitude and generalized weakness. He had lost 18 lb. (8 kg.) during the six months prior to admission.

At the time of admission his blood pressure was 130/70 mm. Hg in the left arm and unobtainable in the right arm. No pulses were palpable in the right upper extremity. In the neck, subclavian and carotid pulsations were absent on the right but present on the left side. The temporal artery pulse was absent on the right but present on the left. Venous filling was diminished over the right forehead and in the right arm. On funduscopic examination only early arteriosclerotic changes were noted. Positive neurological signs were confined to the right arm and consisted of absence of deep tendon reflexes, with an area of anesthesia over the antecubital space. The right arm and forearm were easily fatigued on exercise, but no atrophic changes were observed.

Laboratory studies revealed the hematocrit value to be 45%; hemoglobin level 15 gm. per 100 ml.; and leukocyte count 8,500 per cubic millimeter, with 63% neutrophils, 3% stab cells, 32% lymphocytes, 1% monocytes, and 1% eosinophils. The specific gravity of the urine was 1.008 on two occasions. The blood urea nitrogen level was 9 mg. per 100 ml. A Venereal Disease Research Laboratory flocculation test and a Kahn precipitation test were nonreactive on two occasions. Results of a Treponema pallidum immobilization test were negative. Electrocardiographic tracings were within normal limits. No abnormalities could be detected in routine roentgenograms of the chest. An aortogram made after intravenous injection of sodium acetrizoate (Urokon sodium) demonstrated complete occlusion of the innominate artery near its origin and patent left common carotid and subclavian arteries (fig. 1). Oscillographic and plethysmographic studies showed severe reduction of arterial circulation in the right arm and hand.

A diagnosis of thrombo-obliterative disease involving the innominate artery was made (fig. 1). Although the aortogram did not reveal the distal limits of the occlusive lesion, it was postulated that the obliterative process was segmental in nature and that patency of the peripheral arterial bed existed. It was further assumed that this condition would

probably be found in the subclavian artery just distal to its origin from the innominate and in the internal and external carotid arteries near the bifurcation. Accordingly, at operation on Jan. 4, 1957, the right supraclavicular region was approached first, and through an oblique incision immediately above the clavicle the right subclavian artery was exposed. Palpation revealed no pulsation in the artery, but a compressible lumen was found beginning at about the origin of the thyrocervical trunk. A small arteriotomy in this region confirmed the presence of a patent lumen with good retrograde blood flow. A second small cervical incision was then made to expose the carotid bifurcation. After the right common carotid artery was mobilized for a few centimeters proximal to its bifurcation, and the internal and the external carotid arteries for a similar distance distally, it was found that the thrombotic obliterative process extended throughout the common carotid artery and its bifurcation. Both the internal and external carotid arteries, however, were found to have compressible lumens beginning about 2 cm. distal to their origin. The common carotid artery was then transected at a point approximately 2 cm. proximal to its bifurcation, revealing an organized thrombus filling its lumen. The proximal end was ligated and thromboendarterectomy was performed in the distal end. After removal of this thrombotic process through the carotid bifurcation, a normal lumen was established in this distal segment with vigorous retrograde flow from both internal and external carotid arteries.

Fig. 1.—*A*, aortogram in case 1, after intravenous injection of sodium acetrizoate (Urokon sodium), showing occlusion of innominate artery near its origin and patency of left common carotid and left subclavian arteries. *B*, diagram indicating by shaded area the extent of occlusion.

A right anterior thoracotomy through an incision in the second interspace was then made in order to expose the ascending aorta. The mediastinal pleura was incised and mobilized sufficiently to provide adequate exposure of the ascending aorta. A curved clamp was applied to the anterolateral wall of the ascending aorta, thus excluding a portion of its wall, through which an incision about 3 cm. in length was made. To this aortotomy the trunk of an Edwards-Tapp nylon bifurcation tube was anastomosed, end to side, using a continuous suture of 000 arterial silk (fig. 2). The two limbs of the nylon tube were then passed through the superior mediastinum and the thoracic outlet into the neck. One limb was brought into the supraclavicular incision and anastomosed end to side to the subclavian artery with continuous 0000 arterial silk (fig. 3). The other limb was brought up to the superior cervical incision and anastomosed end to end to the endarterectomized common carotid artery (fig. 4). Immediately after release of the occluding clamps, strong pulsations could be palpated in the subclavian, internal, and external carotid arteries as well as in the right radial and temporal arteries.

The patient made an uneventful recovery and was discharged from the hospital in excellent condition on Jan. 30, 1957. Oscillographic and plethysmographic studies following operation showed striking improvement in circulation to the right upper extremity. An aortogram made after operation revealed the nylon bypass graft to be patent and functioning well, with blood flow to both the subclavian and right common carotid arteries (fig. 5). At the last examination, a little over three months after operation, the patient stated that he was completely relieved of his previous symptoms of claudication in the right arm and that he was again working as a house painter. The right temporal and radial pulses were bounding and blood pressure in the right arm was normal.

Pathological studies of the excised specimen revealed a central core of a somewhat laminated well-organized thrombus with an irregular surrounding layer of intimal proliferation.

Case 2.—A man 47 years old was admitted on March 20, 1957, to Methodist Hospital with the chief complaint of pain in the left arm and shoulder, weakness, and increased fatigability. These symptoms began about 18 months prior to admission. Pain appeared periodically in the region of the head of the humerus and also occurred posteriorly beneath the left scapula. Exercise of the hand and forearm produced pain and aching sensations below the elbow, and any attempt by the patient to work with his hand higher than his head produced a helpless and numb feeling in the left arm. After strenuous exercise in November, 1956, he had aching pain in his left arm and fingers which lasted for two days and was accompanied by considerable soreness of the forearm.

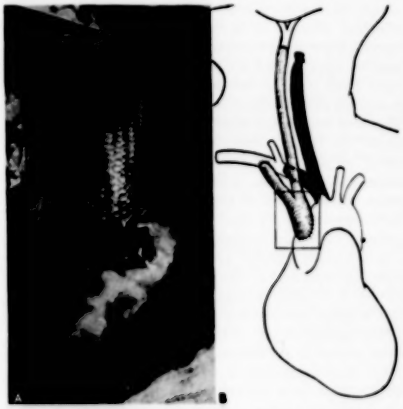

Fig. 2.—*A*, photograph made at operation in case 1, showing end-to-side anastomosis of the nylon bifurcation tube to anterolateral wall of ascending aorta. *B*, diagram illustrating relation of this part of operation (represented in square frame) to distal anastomoses of nylon tube to subclavian and carotid arteries to bypass innominate artery obstruction.

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On physical examination his blood pressure was 130/80 mm. Hg in the right arm. There was evidence of vascular insufficiency in the left hand as manifested by the Allen test. No pulses were palpable at the wrist or in the brachial region, and blood pressure in the left arm was not obtainable. Pulsations in both common carotid arteries were normal. There was no evidence of a Horner's syndrome, and tests for scalenus anticus syndrome were negative. He was otherwise healthy and well developed.

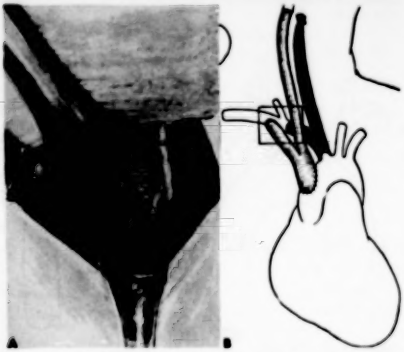

Fig. 3.—A, photograph made at operation in case 1, showing end-to-side anastomosis of one limb of nylon bifurcation tube to right subclavian artery and extension of other limb upward toward carotid bifurcation with vagus nerve lying just medially. *B*, diagram indicating these structures (in framed rectangle) and their relationship to the completed operation.

Laboratory studies revealed a normal hemogram and urinalysis. Serologic tests for syphilis, including the Venereal Disease Research Laboratory test, were negative. Roentgenograms of the chest revealed no cardiac enlargement or abnormality in the superior mediastinum.

A diagnosis of thrombo-obliterative disease of the left subclavian artery was made, and operation was performed on March 21, 1957. With the patient lying in the supine position with his head turned to the right, a left supraclavicular transverse cervical incision was made, and the subclavian and axillary arteries were exposed after dividing the scalenus anticus muscle. The distal portion of the subclavian artery was patent, but a thrombus could be palpated in the proximal undivided subclavian artery. There was adequate flow in the axillary vessel distally and no evidence of arteriosclerotic mural changes. A left anterior incision in the second intercostal space was made and exploratory thoracotomy was performed. The left common carotid artery and aortic arch revealed minimal evidence of atherosclerotic change. The subclavian artery was occluded from its origin at the aortic arch to the level of its first branches, including the internal mammary and vertebral arteries (fig. 6*A*). The aortic arch was mobilized and a traction tape was passed about the arch. A curved arterial clamp was then placed across the base of the subclavian artery, occluding a portion of the aortic arch. The subclavian artery was occluded distally with a bulldog clamp, and an incision was made from the base of the subclavian artery along the course of the thrombus. The thrombus was peeled out of the lumen of the vessel in a satisfactory plane of dissection. A forceful flow of blood was obtained from the distal segment. The arteriotomy incision was repaired with continuous silk sutures (fig. 6*B*). The clamps were released and a satisfactory pulse returned in the left arm. The thoracotomy and cervical incisions were repaired.

The patient's postoperative course was uneventful, and he was discharged from the hospital on March 29, 1957. Immediately after operation the left radial pulse was palpable, and it has since remained normal. Blood pressure in the left arm was also restored to normal (130/80 mm. Hg). The hand and forearm remained warm and caused no further pain. Arteriographic studies following operation demonstrated normal patency of the left subclavian artery. Follow-up examination six weeks after operation revealed the patient to be symptom-free, and he had returned to work.

Histopathological studies of the excised specimen revealed that it consisted of laminated thrombus which was fairly well organized with a surrounding edge of endothelium containing some lipid substances, indicating a moderate degree of intimal proliferation.

Comment

Although the etiology of segmental thrombo-obliterative disease of branches of the aortic arch remains obscure, its pathological features have been well established and are fairly characteristic. In this regard the most important consideration is the fact that the thrombo-obliterative process is well localized, even when it involves all the major branches of the aortic arch. The obliterative lesion usually begins at or near the origin of the great vessels arising from the aortic arch. No case has been encountered in which the aortic lumen has been obliterated. The distal extent of the lesion is variable, but the lesion rarely extends much beyond the bifurcation of the common carotid arteries and the

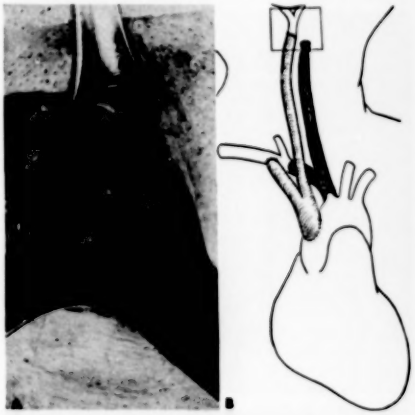

Fig. 4.—A, photograph made at operation in case 1, showing end-to-end anastomosis between one limb of nylon bifurcation tube and distal endarterectomized segment of common carotid artery just proximal to its bifurcation. Hypoglossal nerve may be seen beneath superior retractor. *B*, diagram representing this part of operation (in framed rectangle) and its relationship to completed operation.

supraclavicular portion of the subclavian arteries. Thus, like the Leriche syndrome, the occlusive process is segmented in character, with a patent lumen in the aorta proximally and a patent peripheral arterial bed distally. The significance of this fortunate pathological feature of the disease lies in the fact that it permits direct surgical attack upon the occlusive process in reestablishing arterial continuity and normal circulation.

Several methods of surgical treatment are available for this purpose, namely, thromboendarterectomy, excision with graft replacement, and the use of a bypass graft. The indications for each of these procedures are dependent upon the location, extent, and nature of the occlusive process. In short, well-localized occlusive lesions such as that encountered in case 2, thromboendarterectomy may prove entirely adequate in reestablishing normal blood flow. In most cases, however, the thrombo-obliterative process is likely to be more extensive and tends to involve the entire length of these vessels. Under these circumstances we believe that the bypass is the procedure of choice. For one thing, it has the advantage of simplifying the surgical procedure and minimizing the extent of operative trauma. For another, it is less likely to produce injury or interference with established collateral vessels. In some

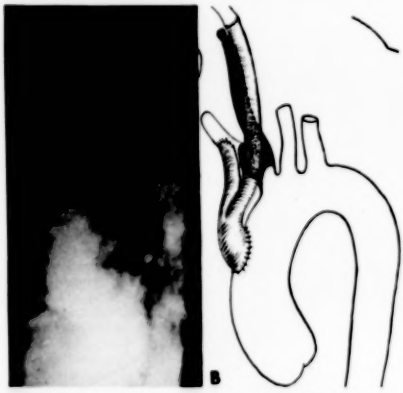

Fig. 5.—A, angiocardiogram made one month after operation in case 1, showing patent and functioning nylon bifurcation tube attached to ascending aorta. *B*, diagram showing relationships.

instances it may be desirable to combine it with thromboendarterectomy of a short distal segment, as illustrated in case 2 described herein. Even in cases in which all of the major branches of the aortic arch are involved, it may be effectively employed simply by attaching additional limbs to the bypass graft. Since a proximal source of blood flow is available from the ascending aorta, the only requirement in the application of this procedure is the establishment of a patent lumen in the arteries distal to the obstruction. This can readily be determined by exposure of these vessels through small incisions in the neck.

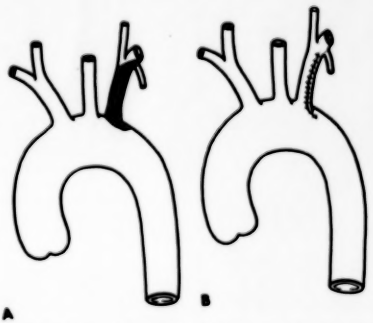

Fig. 6.—Diagram illustrating (*A*) location and extent of thrombo-obliterative lesion (represented by black area) involving left subclavian artery in case 2 and (*B*) operative procedure, consisting of longitudinal arteriotomy, thromboendarterectomy, and suture repair.

Summary

Segmental thrombo-obliterative disease of the branches of the aortic arch, which has also been designated as the aortic arch syndrome, pulseless disease, Takayasu's disease, and Martorell's syndrome, is a clinical entity resulting from occlusion of one or more of the great vessels arising from the aortic arch and characterized by manifestations of ischemic disturbances and absence of pulses in the head, neck, and upper extremities.

Although the etiology of this condition remains obscure, its pathological features are fairly characteristic. Most significant in this regard is the fact that the thrombo-obliterative process tends to be fairly well localized and segmental in character. The occlusive lesion usually begins at or near the origin of the great vessels arising from the aortic arch and rarely extends much beyond the bifurcation of the common carotid arteries or the supraclavicular portion of the subclavian arteries. This fortunate pathological feature of the disease thus permits direct surgical attack upon the lesion in reestablishing normal circulation.

Surgical treatment was successfully applied in two cases, in one by the use of the bypass principle and in the other by thromboendarterectomy. In both of these cases surgery was followed by complete relief of symptoms and restoration of normal circulation.

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CARDIAC OUTPUT AND TOTAL PERIPHERAL RESISTANCE IN ANESTHESIOLOGY

CLINICAL APPLICATIONS

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Total peripheral resistance is defined and measured in terms of the force required to maintain blood flow from the root of the aorta to the venous exit into the auricles. Observing changes only in blood pressure and heart rate may not suffice in the management of anesthesia for complicated and prolonged operations in "poor-risk" patients. In these difficult situations the most important problems are the prevention and treatment of circulatory derangements. The stroke-volume (pulse-pressure) formulas are ideal for the investigation of problems involving acute fluctuations in blood pressure. The clinical anesthesiologist can estimate cardiac output and total peripheral resistance with ordinary clinical data. The most valuable clinical application of the stroke-volume formulas has been to evaluate and interpret the pressor effect of 90-degree passive elevation of the lower extremities (the "L" position or maneuver). The "L" maneuver is a clinical aid in the management of cardiovascular changes associated with anesthesia.

Surgical anesthesia is an experiment in physiology and pharmacology. Even the expert anesthesiologist is often perplexed in attempting to coordinate the multitude of isolated facts related to the patient's preoperative disease and condition, surgical stimuli and positions, deviations of blood volume, derangements of water, mineral, and carbohydrate metabolism, variations in temperature, and changes induced by anesthetic agents and techniques. It is a tribute to clinical art that the anesthesiologist can depend on such simple data as changes in blood pressure and heart rate to comprehend the net circulatory changes resulting from the great number of external influences imposed by the surgeon and anesthesiologist multiplied by the complex variety of internal responses of the patient.

The usual data may not suffice, however, in the management of anesthesia for more complicated and prolonged operations in "poor-risk" patients. In these difficult situations the most important problems are the prevention and treatment of circulatory derangements. Despite much recent progress in anesthesiology, the treatment of hypotensive states is still frequently unsatisfactory, as evidenced by the wasteful or harmful abuse of transfusions, the nonspecific "shotgun" administration of arterenol, and the failure to recognize myocardial insufficiency during operation. Apparently we still often need more refined data for prompt and decisive diagnostic and therapeutic opinions in cardiovascular anesthesiology. Such clinical information may be obtained by the application of studies of cardiac output and total peripheral resistance.

Valuable contributions to this field have been produced with methods and concepts generated by the pioneer work of Cournand and his associates in

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1942. They revolutionized human cardiovascular physiology in applying cardiac catheterization and the direct Fick principle to man. Direct Fick methods then served in calibrating and evaluating other methods of measuring cardiac output and total peripheral resistance, viz., (1) indirect Fick methods, employing carbon dioxide or acetylene; (2) dye-dilution; (3) ballistocardiograph; and (4) pulse-pressure (stroke-volume) formulas.

Many anesthesiologists and physiologists have analyzed the hemodynamic effects of anesthetic agents and methods in man [1] with use of the direct Fick, dye-dilution, or ballistocardiographic methods. The pulse-pressure formulas developed by Remington and his co-workers [2] and Starr and his associates [3] have not been utilized by anesthesiologists.

In 1956 the two blood pressure methods of estimating cardiac output were applied in excellent studies by two independent teams of expert investigators. Assali and his associates employed a formula of Starr in investigating the hemodynamic effects of reserpine and Veratrum drugs.[4] Hendricks and Quilligan based a superlative study of cardiac output during labor on the pulse-pressure method of Remington and Hamilton.[5] Both groups found results consistent with the data that they obtained with a laboratory method of measuring cardiac output.

The stroke-volume (pulse-pressure) formulas are ideal for the investigation of problems involving acute fluctuations in blood pressure. Anesthesiologists are primarily interested in obtaining values of cardiac output and total peripheral resistance which show transient trends and variations in relation to drugs, surgical positions, and other factors acting on an individual patient during a given operation. Absolute values of cardiac output and total peripheral resistance are less important than continuous and immediately comparable values. For this clinical purpose one requires only the accurate measurement of blood pressure and the formulas of Starr or Remington. How well the results satisfy the need depends upon one's viewpoint. If workers with the ballistocardiogram obtained results of similar accuracy they would be quite content.[2b] The experimental investigator may find the pulse-pressure methods leave much to be desired. For the clinical anesthesiologist, however, they "furnish a great deal of useful information as to the direction and general magnitude of cardiac output changes. After all, the flow changes with which he is most concerned tend to be larger than the intrinsic error. In case of critical or small changes in flow, corroborative support from a direct cardiac output determination would, of course, be necessary." [2b]

The accuracy of the blood pressure methods compares favorably with the more complicated direct Fick and dye-dilution methods, especially for clinical application. Comparison of the dye injection and the direct Fick method has shown variations up to 25%.[6] The direct Fick method contains an intrinsic error of 15 to 20%.[3] The Remington method has agreed within 25% with the dye-dilution method in 27 out of 30 observations and within 26% with the direct Fick method.[2a] The formulas of Starr estimate levels of cardiac output below that given by Fick and dye methods but approximate closely the levels obtained by the acetylene, nitrous oxide, and ethyl iodide methods. The trend and percentage change of cardiac output with the Starr formulas are the same as those obtained by the direct Fick method. The same conclusions have always been drawn from any study in which the Starr method has been compared with cardiac output measurements secured by elaborate cardiac output methods.[3] As expressed by Starr [3]

> . . . a rough cardiac output method is now available, so simple that it can be applied by any physician with the apparatus he now has, and . . . its results correlate reasonably well with those secured by the elaborate cardiac output methods in a wide variety of clinical and physiologic conditions . . . this simple method will suffice to measure cardiac output in most clinical conditions with an accuracy commensurate with our present ability to use this knowledge to the advantage of our patients . . . Indeed means are now available to make a rough estimation of cardiac output as a routine part of every examination of the patient, and that physicians taking the blood pressure routinely can interpret their findings with greater insight into their physiologic meaning.

This report has two objectives: first, to demonstrate the value of the stroke-volume (pulse-pressure) formulas as investigative tools in the hands of the clinical anesthesiologist; secondly, to illustrate the application of data based on studies of cardiac output and total peripheral resistance to the better management of problems in the practice of anesthesiology.

Basic Physiology

Determinations of arterial blood pressure and heart rate are only reflections of the fundamental factors, cardiac output and total peripheral resistance: $BP \propto CO \times TPR$. Cardiac output, expressed in milliliters per minute, is the minute volume of blood ejected by a ventricle, i. e., the stroke volume $\times$ heart rate. The stroke volume of the average healthy man is 70 to 80 ml., although each ventricle has a normal capacity of approximately 200 ml. and contains about 100 ml. of residual blood at the end of systole. The minute volume under basal conditions varies from 3 to 4.6 liters by the Grollman acetylene method or 5.5 liters by the Cournand direct Fick method. When expressed in relation to surface area, cardiac output becomes cardiac index; it averages 2.2 liters per square meter (Grollman) or 3.3 liters per square meter (Cournand). Like basal metabolism, cardiac output is proportional to surface area in normal persons and may be approximated with a small error by the use of average body

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surfaces, 1.8 square meter (male adult) and 1.6 square meter (female adult). In proportion to weight, cardiac output averages 62 ml. per kilogram per minute.

Total peripheral resistance is defined and measured in terms of the force required to maintain blood flow from the root of the aorta to the venous exit into the auricles. In clinical anesthetic situations, the only important factor in total peripheral resistance is the arteriolar bed. Total peripheral resistance varies directly with the mean blood pressure and inversely with the rate of blood flow, i. e., CO. TPR is calculated by dividing the mean blood pressure (diastolic pressure + ⅓ pulse pressure) by the cardiac output per second and multiplying the ratio by 1,332 in order to reduce it to the conventional unit of dynes per second per centimeter, which is also termed "absolute unit of force" (a. u.).

$$\text{TPR (in dynes/sec./cm.)} = \frac{\text{mean BP in mm. Hg}}{\text{CO in cm.}^3\text{ per sec.}} \times 1{,}332$$

$$= \frac{\text{mean BP in dynes/cm.}^2}{\text{CO in cm.}^3\text{/sec.}}$$

$$= \frac{\text{DP} + \frac{1}{3}\text{ PP}}{\text{CO per sec.}} \times 1{,}332$$

In normal man, total peripheral resistance averages 1,250 a. u., with a range of 600 to 2,000 a. u.; it may be as high as 5,000 in hypertensive disease.

Formulary Methods of Estimation of Cardiac Output

Since total peripheral resistance is measured in terms of arterial blood pressure and cardiac output, and since cardiac output is satisfactorily computed for clinical purposes from arterial blood pressures, the clinical anesthesiologist can estimate cardiac output and total peripheral resistance with ordinary clinical data.

Starr's formulas for the estimation of cardiac output, based on auscultatory blood pressure readings, are as follows:

When the disappearance of sounds is used to indicate diastolic pressure, Starr's formula for the estimation of cardiac output is his equation 72,[3] namely,

Stroke volume (cc.) = 100 + 0.5 pulse pressure − 0.6 diastolic pressure − 0.6 age (yr.)
Cardiac output = stroke volume × heart rate

When the point of muffling of sounds is taken to indicate diastolic pressure, Starr's formula is his equation 68,[3] namely,

Stroke volume (cc.) = 93 + 0.54 pulse pressure − 0.47 diastolic pressure − 0.61 age (yr.)
Cardiac output = stroke volume × heart rate

Wherever possible an average of multiple determinations of blood pressure is used to increase the accuracy of the estimate of cardiac output.

The estimation of cardiac output by the method of Remington and Hamilton also uses auscultatory determinations of arterial blood pressure.[24] The formulas and table of corrected "volume factors" are as follows:

Pulse pressure is corrected for body size and for inflections in the aortic distensibility curve by the "volume factors" in the table. For each systolic and

Factors for the Prediction of Stroke Volume, Per Square Meter of Body Surface, from the Pulse Pressure[a]

Pressure, Mm. Hg	Vol. Factor, Cc.	Pressure, Mm. Hg	Vol. Factor, Cc.	Pressure, Mm. Hg	Vol. Factor, Cc.
20	0	100	81	180	140
30	10	110	90	200	148
40	21	120	100	220	155
50	31	130	108	240	161
60	42	140	115	260	167
70	52	150	122	280	173
80	62	160	128	300	179
90	71	170	134		

[a] Reference 2a, page 395.

diastolic pressure the corresponding volume factor is substituted. Thus, systolic pressure 120 mm. Hg when corrected becomes 100 and diastolic pressure 82 mm. Hg when corrected becomes 64; therefore the corrected pulse pressure becomes 36.

Cardiac index = corrected pulse pressure × heart rate
Cardiac output = cardiac index × body surface in square meters

The calculation of cardiac output from cardiac index is unnecessary when the primary interest is to study changes within a single patient under influence of various conditions of anesthesia, with the patient serving as his own control. When cardiac output is desired for comparison with other methods of measuring cardiac output, the cardiac index must be multiplied by body surface to convert it into cardiac output.

Clinical Applications

Estimation of Cardiac Output and Total Peripheral Resistances in Specific Clinical Anesthetic cases.—The accompanying graphs (fig. 1 and 2) illustrate the application of Starr's formula (equation 72) to the estimation of cardiac output and total peripheral resistance every five minutes during anesthesia. The circulatory changes in hyperthyroidism and spinal anesthesia were chosen as examples because they are well known and, therefore, the results of our analysis can be better appreciated for their validity and value. The graphs clearly demonstrate characteristic trends and the general magnitude of cardiac output and total peripheral resistance.

Figure 1 graphically shows the extremely high cardiac output and low total peripheral resistance characteristic of severe thyrotoxicosis, despite preparatory hospitalization, thorough antithyroid medication, and effective preoperative sedation. The surgeon gave me the responsibility of the decision

to proceed with anesthesia and operation. I then depended on the patient's response to induction of anesthesia with an intravenously given barbiturate, in this case methitural sodium. The fall in cardiac output and rise in total peripheral resistance were typical and expected and, in this case, sufficiently impressive to favor the choice of continuing with anesthesia and operation. Thereafter cardiac output was kept down by the following measures: (*a*) orotracheal intubation to reduce dead space, (*b*) semiclosed circle system of carbon dioxide absorption and administration of 6 liters of nitrous oxide and 3 liters of oxygen to minimize the rise of cardiac output and total peripheral resistance due to hypercapnia, (*c*) maintenance of basal anesthesia with

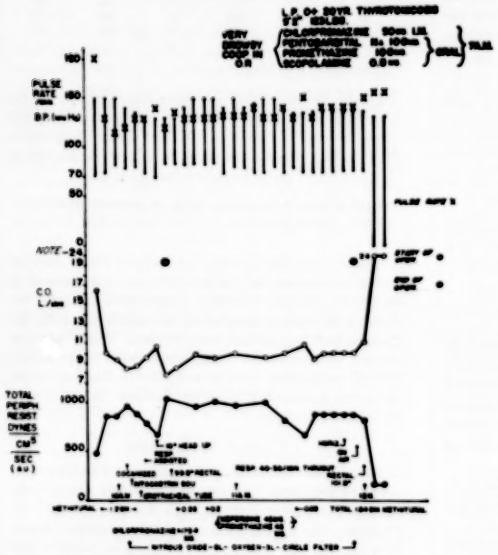

Fig. 1.—Circulatory changes in thyrotoxicosis, thiopental anesthesia, head-up position, and posthypercapnia.

intravenously given thiobarbiturate, meperidine, chlorpromazine, and promethazine, (*d*) 10-degree head-up tilt (note the physiological fall in cardiac output and rise in total peripheral resistance expected of this position).

When the patient was permitted to breathe air, total peripheral resistance fell steeply to a very low level and cardiac output physiologically rose in a compensatory response to maintain an adequate level of mean arterial blood pressure. The sharp fall in total peripheral resistance is characteristic of the immediate posthypercapnic state, as will be shown later. The patient convalesced without crisis, probably because of effective lowering of metabolism and cardiac output with icebags and thorough morphinization, and high oxygen inhalation therapy to meet metabolic need.

Figure 2 portrays the routine circulatory events of spinal anesthesia for inguinal herniorrhaphy in a healthy 29-year-old male. The fall in cardiac output and rise in total peripheral resistance are as typical of spinal anesthetic hypotension as is the bradycardia. The 90-degree leg-raising maneuver clearly raises cardiac output while total peripheral resistance is little affected.

Investigation of Uncertain Circulatory Effects of Anesthetic Agents and Techniques.—Investigation of anesthetic agents and techniques revealed the following circulatory effects.

Spinal Anesthesia: The generally accepted explanation of spinal hypotension is arteriolar dilatation in the anesthetized area due to paralysis of vasoconstrictor fibers in the anterior spinal nerve roots.[1b] On the other hand, there is excellent evidence for the primary cause being reduced cardiac output resulting from postarteriolar pooling of blood.[7] The stroke-volume formulas readily provide a clinically useful answer. As a rule, in spinal anesthesia systolic and pulse pressures fall more markedly than diastolic pressure, while the pulse rate is unchanged or decreased. With such data, calculation from a pulse-pressure formula shows a reduction in cardiac output (fig. 2). This conclusion is supported by our experience with the 90-degree leg-raising test which has always demonstrated a pressor effect and revealed venous pooling in spinal hypotension, unless myocardial failure or hypovolemia had supervened to complicate the problem. In a minority of cases, however, decreased total peripheral resistance may accompany a fall in cardiac output, particularly when preexisting total peripheral resistance was high.[7] Occasionally, decreased total peripheral resistance is more important than decreased cardiac output, more commonly in hypertensive patients and especially when the vasovagal phenomenon supervenes.[8] By calculation from the pulse-pressure formulas such variations may be detected.

Carbon Dioxide Effect: The pressor effect of mild to moderate degrees of hypercapnia during general anesthesia is well known but the mechanism is not. It has been attributed to stimulation of cardiac output or central increase of arteriolar constriction, or both. When cardiac output and total peripheral resistance are estimated from the usual clinical signs

of hypercapnia, viz., marked rise in systolic and pulse pressures, moderate rise in diastolic pressure, and rapid or slow heart rate, the results are that total peripheral resistance is always increased markedly while cardiac output may be increased, unchanged, or decreased (fig. 3).

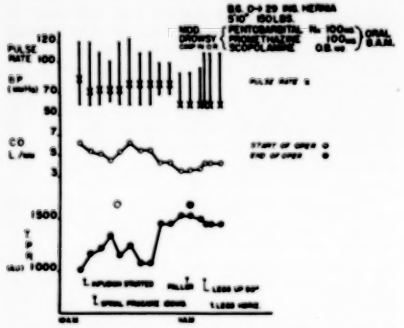

Fig. 2.—Circulatory changes typical of spinal anesthetic hypotension and 90-degree leg raising.

Posthypercapnic Hypotension: Data on the changes in cardiac output and total peripheral resistance in this common type of hypotension are meager. The usual observations are marked falls in systolic and diastolic pressures and a slow or rapid heart rate. When cardiac output and total peripheral resistance are calculated for the periods just before and after the fall in arterial pressure, the constant finding is a sudden reduction of the previously elevated total peripheral resistance (fig. 1 and 3). Cardiac output in the immediate posthypercapnic period frequently is elevated but soon falls; the changes in cardiac output often fail to offset the decline in total peripheral resistance. Regardless of the level of arterial pressure, the leg-raising maneuver has a pressor effect and thereby reveals venous pooling; apparently widespread venodilatation accompanies the extreme arteriolar dilatation.

Formulation of Ninety-Degree Elevation of Lower Extremities as a Test of Circulatory Function.—The most valuable clinical application of the stroke-volume formulas in my own practice has been to evaluate and interpret the pressor effect of 90-degree passive elevation of the lower extremities (hereafter termed the "L" position or maneuver).

Many physiologists and anesthesiologists have long recognized the value of this postural maneuver in hypotension caused by spinal [9] and thiopental anesthesia.[10] Conflicting explanations attribute the mechanism responsible for the effect of the "L" position either to a change in cardiac output caused by increased venous return [7] or to an increase in total peripheral resistance.[8a] By rigidly standardizing the performance of the "L" maneuver, stressing the importance of abrupt leg elevation and accurate measurement of systolic and diastolic pressure and pulse rate during the first 30 seconds, by applying the "L" position at every opportunity in many hundreds of cases during the past four years and carefully recording the changes, I have gathered a substantial body of data which may be summarized as follows:

1. In 300 recumbent, rested normal subjects the "L" maneuver did not significantly affect systolic or diastolic pressure or heart rate. Therefore we may conclude that normal cardiac output and total peripheral resistance are not influenced to a clinically detectable degree by leg raising.

2. When the "L" maneuver significantly raised arterial pressure, systolic pressure rose more than 10 mm. Hg; diastolic pressure and heart rate were changed little and inconstantly. Reasoning from the pulse-pressure formulas, the pressor mechanism of leg-raising is a rise in cardiac output, undoubtedly due to increased return of pooled blood in the post-arteriolar bed of the lower extremities. The pressor effect appears within 5 to 10 seconds and is therefore largely derived from emptying of veins.

3. In hypotensive states caused purely by spinal (400 cases), epidural (28 cases), or intravenously administered barbiturate anesthesia (100 cases), the "L" position consistently revealed the presence of venous pooling and inadequate cardiac output.

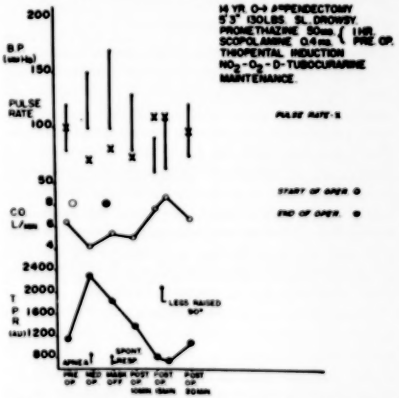

Fig. 3.—Circulatory changes in carbon dioxide retention followed by posthypercapnia hypotension. Note effect of 90-degree leg raising.

4. In 12 patients with simple vasovagal syncope and 27 "idiopathic" hypotensive patients, the "L" maneuver did not elevate arterial pressure. The mechanism of hypotension was therefore not related to a reduction in cardiac output by venous pooling.

Since cardiac disease was absent, the inference may be drawn that hypotension in these two syndromes was due to reduced total peripheral resistance.

5. In hypotension produced solely by premedication with meperidine or morphine (147 cases), the "L" maneuver always had a systolic pressor effect, demonstrating the underlying reduction of cardiac output due to venous pooling.

6. In 176 patients with uncomplicated posthypercapnic hypotension, the "L" maneuver likewise caused significant systolic elevation. While venous pooling and inadequate cardiac output were important factors, the primary cause of posthypercapnic hypotension, as shown earlier in this report, is reduced total peripheral resistance.

7. The "L" maneuver had no significant effect on blood pressure and heart rate in hypotension produced by intravenously administered chlorpromazine (20 to 50 mg.) in 10 normal subjects. This "negative" response pointed to reduced total peripheral resistance as the primary mechanism of hypotension with chlorpromazine, as recently shown by Etsten and Li.[18]

8. In hypotensive states primarily associated with reduced cardiac output due to venous pooling, e. g., thiopental or spinal anesthesia, the normally expected systolic pressor effect of the "L" position was not obtained when blood loss exceeded 750 to 1,000 ml. (observations based on 74 patients) or when myocardial failure was present (4 patients).

Comment

My experience with the pulse-pressure formulas confirms their usefulness for our purpose. They have led to correct approximate conclusions regarding the general trend of cardiac output and total peripheral resistance in anesthetized patients. The formulary methods have their limitations and exceptions, especially in patients with myocardial failure and other organic cardiovascular abnormalities. On the other hand, the value of formulary methods will not be underestimated if one is aware that even the dye-dilution and direct Fick methods are not sufficiently reliable to permit firm deductions from small changes in single individuals.

Although estimates of cardiac output and total peripheral resistance with a formulary method may not be conclusive in every instance, a great deal of useful and stimulating information can readily be obtained from one's daily cases. Not the least of the benefits is the enlarged viewpoint that results from the knowledge of changes in cardiac output and total peripheral resistance produced by drug, position, technique, or surgical manipulation. Examples of such considerations are as follows:

1. The increase in cardiac output by atropine [11] favors its use when a fall in cardiac output is to be minimized.

2. For patients susceptible to shock, the marked tendency of cyclopropane to increase total peripheral resistance [16] is far more desirable than spinal and intravenous barbiturate anesthesia, which regularly reduce cardiac output. For the same reasons, however, the latter anesthetics are more suitable for "hypotensive anesthesia." Indeed, reduction in cardiac output is more important than reduction in total peripheral resistance or the level of arterial blood pressure in minimizing surgical hemorrhage.[12]

3. For premedication or antiemesis, promethazine, which does not significantly change cardiac output and total peripheral resistance,[12] is preferred to chlorpromazine except when the specific effect of the latter in decreasing total peripheral resistance [18] is sought in lowering blood pressure or body temperature.

4. Elevation of total peripheral resistance and cardiac output by retained carbon dioxide must be expected and evaluated whenever general anesthetic effects on circulation are considered.

5. Ephedrine frequently fails as a vasopressor in spinal hypotension, especially when the reduction in cardiac output responsible for hypotension is associated with a mechanical factor interfering with venous return, e. g., full-term uterus, a flexed, prone, or hyperextended surgical position, surgical pads or retractors. When cardiac output is reduced because of inadequate venous return, the inotropic and chronotropic effects of ephedrine frequently fail to augment stroke volume and cardiac output while the total peripheral resistance falls with ephedrine.[14] The desirable vasopressors, then, are phenylephrine and methoxamine, which increase vasomotor tone, particularly in the veins where pooling of blood occurs in spinal anesthesia.

6. The patient with the mechanical interference of mitral or aortic stenosis cannot increase left ventricular output called for by a reduction in total peripheral resistance. In the choice of anesthetic agents and management one should therefore avoid factors which reduce total peripheral resistance or increase cardiac output. Otherwise pulmonary edema may follow in the wake of the increased amount of blood trapped in the pulmonary vasculature or, on the other hand, shock may result from the uncompensated reduction in total peripheral resistance.

The most practical result of these efforts at clinical detection of significant changes in cardiac output and total peripheral resistance has been the evaluation of the "L" maneuver as a clinical aid in the management of cardiovascular changes associated with anesthesia. The reliability and practicability of the "L" maneuver place it in the same category with analogous tests of circulatory function as the Valsalva and the "tilt-back overshoot" maneuvers.

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The results of the 90-degree leg-raising maneuver may be summarized as follows:

1. A quick, early rise (fleeting or sustained) in systolic pressure greater than 10 mm. Hg is unequivocal evidence of a rise of cardiac output and reveals venous pooling. It is present ("positive") in hypotensive states, absolute or relative, produced by morphine, meperidine, barbiturates, the post-hypercapnic state, and spinal and epidural anesthesia. 2. At normotensive and hypertensive levels the "L" maneuver normally has no effect; if venous pooling is present, however, the "L" maneuver is "positive." 3. The absence of a significant effect by the "L" maneuver during hypotension, absolute or relative, indicates the absence of venous pooling. This "negative" response to 90-degree leg raising occurs in three types of hypotensive states: (1) hypovolemia, (2) myocardial failure, and (3) those usually caused by reduced total peripheral resistance, e. g., by chlorpromazine, vasovagal syncope, hyperpyrexia.

From the data gathered for this report and the published studies of others it is quite clear that venous pooling, with or without reduction in cardiac output, is an extremely common phenomenon. Long before laboratory evidence for this conclusion was accumulated surgeons had clinically established the value and universally adopted the safeguard of the Trendelenburg position. Emphasis on the "head-down" rather than the "feet-up" part of the position has been the custom because the former supposedly assures an adequate cerebral blood supply by the oversimplified logic of utilizing gravity to divert circulatory blood volume to the brain. Without the handicaps of the "head-down" position to pulmonary function, elevation of the lower extremities, especially when placed far above the usual maximum of 30 degrees used with Trendelenburg position, is undoubtedly far more effective in correcting the vast majority of circulatory derangements during anesthesia and the immediate recovery period.

The control of venous pooling and cardiac output has been studied by Smirk and Restall with water immersion and mechanical devices to lower and raise arterial blood pressure during various types of vasomotor depression and by Gardner and Dohn with the application of 10 to 20 mm. Hg pressure to the lower half of the body of anesthetized patients.[15] Since Estes and associates have shown that total peripheral resistance is not significantly altered by inflation of an antigravity suit to 60 mm. Hg within 10 seconds,[16] it seems likely that changes in cardiac output dominate the fluctuations of arterial blood pressure caused by mechanical measures applied during the venomotor depression characteristic of most anesthetic agents and methods. A counterpressure garment promises to become a convenient means of utilizing the circulatory advantages of the "feet-up" or "L" position during operation.

Summary

The value in cardiovascular anesthesiology of pulse-pressure (stroke-volume) formulas for the estimation of cardiac output and total peripheral resistance has been demonstrated by analyzing, comparing, and graphing the trend and general magnitude of changes in cardiac output and total peripheral resistance in three cases. The effect of 90-degree elevation of the lower extremities has been analyzed in terms of changes in cardiac output and total peripheral resistance. The "L" maneuver demonstrates the widespread occurrence of venous pooling and reduced cardiac output during and immediately after anesthesia. The "L" maneuver has been formulated as a diagnostic test. As a prophylactic and therapeutic measure the "L" position, or its equivalent in the counterpressure garment, is preferred to the "head-down" position.

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AIDS IN EARLY DIAGNOSIS OF TUMORS ON TIP OF NOSE

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Of 95 soft tissue tumor lesions at the tip of the nose on which a biopsy was done, 58% were basal cell epitheliomas, and 21% of these were missed clinically. Difficulty in clinical diagnosis may be due to the fact that the skin over the tip of the nose is thick, adherent to underlying cartilages, and abundantly supplied with sweat and sebaceous glands. Final diagnosis must be made by skin biopsy which reveals the cytology, the architecture, and also the depth to which a neoplasm has invaded the integument.

In our experience, an early accurate clinical differential diagnosis of soft tissue tumors about the tip of the nose is often difficult (fig. 1). Of 95 such lesions on which a biopsy was done at the department of dermatology of the University of Cincinnati, 58% were basal cell epitheliomas, and 21% of these were missed clinically. Seventeen per cent of the nose lesions were dermocellular nevi, and the clinical diagnosis was incorrect in 37% of the cases. Senile keratoses accounted for 5% of our cases. Here again, a 50% discrepancy existed between the clinical and the histological diagnosis. In our series, there were 6% basal cell carcinomas (seborrheic keratoses). The diagnosis was missed in 60% of these cases. Also, 60% of our cases of senile sebaceous hyperplasia and 60% of our cases of squamous cell epithelioma were missed clinically. The table gives the correlation between histological and clinical diagnoses.

Correlation of Histological and Clinical Diagnoses in Ninety-five Lesions of the Nose in Which Biopsy Was Done

Histological Diagnosis	Cases, No.	Clinical Diagnosis Confirmed, %	Incorrect Clinical Diagnosis, %
Basal cell epithelioma	53	79	21
Dermocellular nevus	16	63	37
Seborrheic keratoses	6	50	50
Senile keratoses	5	50	50
Sebaceous adenoma	4	50	50
Squamous cell carcinoma	3	40	60
Verruca vulgaris	3	34	66
Sarcoid	2	100	0
Molluscum contagiosum	1	0	100
Granuloma annulare	1	100	0
Lupus vulgaris	1	100	0

One possible excuse for this difficulty in clinical diagnosis may be the fact that the skin over the tip of the nose is thick, adherent to the underlying cartilages, and abundantly supplied with sweat and sebaceous glands.[1] Also, the rich blood supply of this area tends to increase the difficulties of the clinician. The combination of hypertrophic sebaceous glands, telangiectasia, and a chronic low-grade inflammatory infiltrate frequently seen in individuals in the tumor age group masks a neoplasm that may grow in such an area and distorts its morphology.

Nevertheless, early diagnosis in this area is of paramount importance in the case of neoplasms, not only of the metastasizing type but also of the

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locally malignant kind. The larger the neoplasm, the more disfiguring the treatment whether it be radiologic or surgical. It is, therefore, incumbent on the physician to use every diagnostic tool at his command in order to arrive at a correct diagnosis as early as possible. However, in the last analysis, the accuracy of a test in establishing a tissue diagnosis should determine its choice. Surely one should never destroy a lesion by surgical, chemical, electrosurgical, or radiologic methods without arriving at a diagnosis first.

We have tried to evaluate the various diagnostic procedures available for clinical examination. Of these, inspection with the naked eye with adequate illumination is obviously the first step in the examination, but this method is so frequently misleading that we must resort to other methods. A simple and useful diagnostic tool is the plastic S-shaped diascope,[2] which is of decided value in the differentiation of basal cell epitheliomas from the sebaceous gland hyperplasias so commonly seen in the aging skin (fig. 2). Magnifying glasses or weak power head loups are also of some value in examination, especially for the presbyopic examiner. Goldman has used various types of optical devices in the form of simple and compound microscopes to study the pathological changes in situ in the living skin.[2b] Skin microscopy, with use of

Fig. 1.—Basal cell epitheliomas incorrectly diagnosed clinically.

the portable type of stereobinocular (4× to 15×) with a powerful source of light, is valuable because it shows up more clearly the pearly character and the telangiectasia of early basal cell epitheliomas on the tip of the nose.

The recognition of pigmented nevi of the mixed and junctional types is facilitated by skin microscopy which brings out the spotty distribution of the pigment deposits, a phenomenon not evident to the naked eye in most cases. Goldman has shown that even in the presence of scaling in the surrounding skin, seborrheic keratoses do not show scaling. This fact together with the pigmentary changes helps to identify them. Later, in the evolution of seborrheic keratoses, the keratotic plugs and rugose surface as seen under the skin miscroscope help to distinguish them from the freckle even before such a differentiation can be made by inspection or by palpation. However, skin microscopes are usually not readily available, nor do most dermatologists have experience in the use of these.

Fig. 2.—*A*, basal cell epithelioma of nose. *B*, same lesion under diascope. *C*, skin microscopy. *D*, 1.5-mm. punch biopsy.

The final diagnosis must be made by skin biopsy which reveals the cytology, the architecture, and also the depth to which a neoplasm has invaded the integument. In the case of the individual who refuses biopsy, skin microscopy must suffice. Exfoliative cytology has some value, particularly in viral and bullous disorders of the skin, but work in the department has shown that for solid tumors of the

skin, curettage with study of cytology has not been of practical value. Skin biopsy must provide adequate material if it is to be of diagnostic significance, even though the structure of the nose precludes the performance of extensive excision biopsies. After excision closure is difficult because of the friability of the skin of the bulbous portion of the nose with its abundance of sebaceous glands. At times, hemorrhage following deep biopsy is disturbing.

city (fig. 3). They can be done with a minimum expenditure of time in the office and without operating room facilities or trained assistants.

The 1.5-mm. punch does not yield sufficient tissue for diagnosis unless one penetrates sufficiently. The cylinder of tissue is difficult to pick out of the wound except when it is of adequate length. If not, it tends to fragment. There is frequently some compression of tissue with disortion of cells, which can be obviated to some extent by attaching the punch

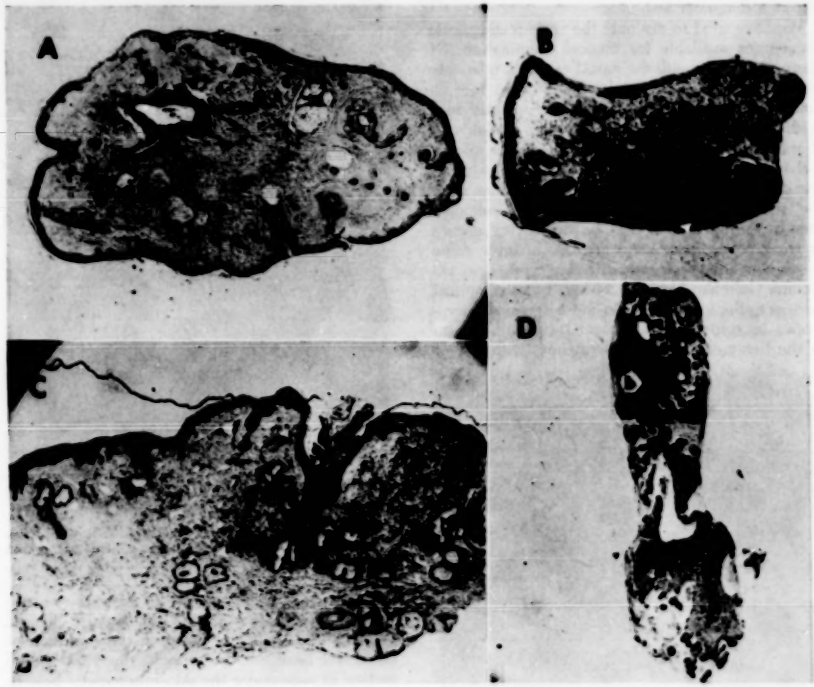

Fig. 3.—Biopsy material obtained by, *A*, scissors; *B*, 2-mm. punch; *C*, Bard-Parker no. 15 blade; and, *D*, razor blade.

We have tried to obtain biopsy material by using various techniques in order to discover those which fulfill our purpose best. What we really need is a biopsy technique to give us adequate diagnostic material with negligible scarring. The following are the biopsy techniques which we have employed: (1) 1.5-mm. punch, (2) 2-mm. punch, (3) scissors biopsy, (4) razor blade biopsy, and (5) biopsy with no. 15 Bard-Parker blade. We have been able to obtain adequate amounts of tissue with every one of these methods, and all have the virtue of simplito a motor-driven shaft. This enables a speedy cutting without compression or tearing of tissue. Moreover, local infiltration of procaine is unnecessary when a mechanically driven punch is used.

The 2-mm. punch produces compression less commonly, making it easier to pick out the tissue, furnishing more material, and producing cicatrization that is hardly noticeable. Scissors biopsy is suitable in certain cases. The razor blade and the Bard-Parker no. 15 blade cut a thin sliver of tissue of any desired depth, including portions of both the

lesion and the healthy surrounding skin. We find that a small piece of a razor blade held with a hemostat makes an excellent instrument for this purpose. Pressure downwards and laterally on each side of the biopsy site with cotton-tipped applicators gives both hemostasis and sufficient retraction of the wound edges to enable the operator to pick up the sliver of tissue and to snip it off. Healing is rapid and the scar is very fine.

Summary

The anatomy of the tip of the nose makes early diagnosis of small soft tissue tumors difficult. Clinical inspection, diascopy, and skin microscopy all help to some extent, but an adequate biopsy is still the best aid. There are various difficulties in performing a biopsy in this area, but small deep biopsies can be done with good cosmetic results.

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VALVULOPLASTY FOR MITRAL STENOSIS DURING PREGNANCY

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The occurrence of pregnancy in a patient with mitral stenosis measurably increases the demands on the heart. In handling this situation a place exists for medical therapy, therapeutic abortion, and surgical intervention, depending on the individual case. The results of mitral valvuloplasty during pregnancy in 27 patients are here reported. There were 3 maternal deaths, 1 failure to improve, and 23 moderate to marked improvements. Analysis of the causes of maternal death suggested more stringent criteria for the selection of patients, especially the elimination of patients with free mitral insufficiency. There were six fetal deaths. Twenty children, including one set of twins, were born by pelvic delivery, and one was delivered by cesarean section because of breech presentation; in addition, six normal children have been born in subsequent pregnancies. The twins were born spontaneously at term to a mother who, having miscarried in four previous pregnancies, underwent a valvuloplasty in the third month of her fifth pregnancy.

Organic heart disease continues to be a serious complication of pregnancy. Its incidence is variously reported between 0.3 and 2%, with a 2 to 3% maternal death rate even under favorable circumstances.[1] Eighty-five to ninety-five per cent of such heart disease is rheumatic in origin,[1] and in 75% mitral stenosis is dominant. Among Burwell's [2] 178 cases, 125 had mitral stenosis, 39 mitral insufficiency, 8 aortic insufficiency, and in 6 aortic stenosis was dominant. The obvious preponderance of mitral stenosis as a problem in pregnancy emphasizes the need for a reassessment of medical therapy, therapeutic abortion, and the surgical correction of mitral stenosis during pregnancy.

Hemodynamic Considerations

In its simplest form, the hemodynamic problems caused by mitral stenosis are due to a reduced fixed orifice requiring increased left atrial diastolic pressure to maintain an adequate forward flow. The increased left atrial pressure is reflected back into the pulmonary vascular bed, with resulting pulmonary hypertension. It is manifested clinically by

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dyspnea, orthopnea, episodes of paroxysmal dyspnea, frank pulmonary edema, or eventual right ventricular failure.

Demands for greater cardiac output may result in further increase in left auricular and pulmonary pressures. Tachycardia as a mechanism of increasing cardiac output is notably disadvantageous in the presence of severe mitral stenosis. As we have previously observed,[3] the paradoxical and deleterious effects of tachycardia are due to a combination of three factors. First, tachycardia reduces the total diastolic time. There is less opportunity for auricular and pulmonary drainage into the ventricle. Second, in the presence of any associated mitral incompetence, the number of regurgitant jets is increased with concomitant increase in the total volume of reflux. Third, the right ventricle, if competent, tends to deliver greater blood volume to the lungs. The first two factors increase left auricular congestion and thereby aggravate pulmonary hypertension. Whether or not this leads to an increase in pulmonary vascular resistance, the three factors combined produce a second point of obstruction to effective circulation in the lungs.

The physiological changes associated with pregnancy admirably studied by Hamilton [4] and by Burwell and his associates [5] impose a special burden on patients with mitral stenosis. Among these changes are (1) an increase in oxygen consumption approximately 20% above basal levels, (2) a rise in basal heart rate, (3) an increase in cardiac output out of proportion to oxygen consumption that may amount to 40 to 50% at the time of its maximal effect, (4) increased total blood volume, chiefly a function of increased plasma volume which exceeds the red blood cell mass, and (5) increased sodium retention. These changes are maximal about the eighth month of pregnancy (the 32d to 36th week of gestation). Thereafter there is a decline toward normal during the last four weeks of pregnancy. These normal physiological changes in pregnancy will be magnified in a woman already limited by mitral valvular obstruction. An increase in left auricular pressure is generally associated with these changes. If the stress is sufficient, acute and chronic pulmonary hypertension results and the adverse effects of mitral stenosis are accentuated.

The Clinical Problem

Much has been written about the life cycle of mitral stenosis. Noteworthy are the efforts of Olesen [6] and Ellis.[7] The specific problems of mitral stenosis during pregnancy have been emphasized by Hamilton and Burwell.

Three Choices of Management.—It is now well recognized that mitral stenosis diagnosed by murmur alone may be of no hemodynamic significance, irrespective of associated pregnancy. On the other hand, progressive limitation generally in the form of dyspnea and pulmonary congestion can manifest itself at any time. Confronted with evidence of congestive failure early in pregnancy, the physician has three alternatives: 1. He may institute or intensify medical therapy. 2. Pregnancy may be interrupted and mitral stenosis corrected later. 3. Mitral stenosis may be corrected and the pregnancy salvaged.

The first alternative, embracing rigid medical therapy, has a firm place. It should include limitation of activity to the point of bed rest if necessary, digitalization or optimal adjustment of digitalis therapy, strict salt restriction, and the judicious use of diuretic agents. Close supervision at weekly intervals is essential. Any progression of symptoms on such a program warns that this may be too conservative.

Hamilton's [4] figures indicate a substantial maternal and fetal mortality in patients with congestive failure during pregnancy, even under ideal circumstances. Patients in groups 1 and 2 (American Heart Association classification) are exposed to 2.5% maternal mortality. Those with the unfavorable prognosis, as represented by groups 3 and 4, have a 16% maternal mortality. Similarly, infant mortality is appreciably increased, particularly in groups 3 and 4 where this may reach 30% or more despite proper medical therapy.

The second possibility, therapeutic abortion with valvuloplasty later, has been the choice of some when medical therapy proved inadequate. This represents a compromise. Such a decision may be unacceptable to parents eager for children or motivated by religious considerations. To the physician it represents defeat! At best it involves two operations. To be sure, a place for therapeutic abortion exists, and there are circumstances in which a cardiac patient cannot endure the added burden of pregnancy. If the heart disease is not amenable to surgical correction, then interruption of the pregnancy may be indeed lifesaving. This, however, is rarely if ever the case in pure mitral stenosis.

Advocates of interrupting pregnancy [8a] have emphasized the low risk involved in therapeutic abortion during the first trimester. However, some individuals will not show evidence of a failing circulation from the burden of stenosis and pregnancy this early. Yet, during the fourth month the risk of interruption increases significantly. Beyond this time the risk of a major abdominal procedure (hysterotomy) in the presence of a severely compromised heart may well be more than that of correcting stenosis. It is in this latter group that Burwell [8a] has conceded a place for mitral valvuloplasty during pregnancy.

If medical management fails, the third alternative may constitute the best solution. Surgeons faced with this problem have advocated valvular surgery, while physicians have been "less aggressive" yet accepted two operations (first therapeutic abortion then valvuloplasty) or occasionally have held too

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tenaciously to a medical program. The results of a surgical program will be presented below. In addition to the various medical considerations, the problem is often further complicated by religious and moral convictions which cannot be ignored.

Bland [8] has taken the position that surgery for mitral stenosis during pregnancy is unacceptable because of the high operative mortality. He quotes a risk of 15% based on a collected series of operative endeavors. Similarly Burwell mentions two operative deaths in seven operations.[5a] In support of interrupting pregnancy, Burwell [5b] argues as follows: 1. In general, pregnant women who have mitral stenosis do well on medical therapy. He presumes that those who would tolerate surgery would also survive pregnancy on a strict medical regimen. 2. The complexities of the total situation of pregnancy plus mitral stenosis are greater than those of mitral stenosis alone in the nonpregnant state. Valvuloplasty during pregnancy should therefore be more hazardous. 3. The possibility of acute rheumatic fever or rheumatic carditis is present. 4. Finally, even in experienced clinics errors in diagnosis occur.

Merits of Surgical Management.—In reflecting on these arguments and our experience, it seems fallacious to assume that any who could withstand surgery could necessarily go through pregnancy on a medical regimen. The burdens of valvuloplasty and pregnancy are dissimilar in physiological nature, duration, and degree. Finally, patients who have experienced pulmonary edema in the first trimester may respond immediately to surgery, yet notoriously have difficulty if pregnancy and stenosis continue.

Hamilton [9] has recently reaffirmed his position in favor of therapeutic abortion but recognizes the possibility that improved management and surgical techniques might necessitate a revision of this attitude. Glover [10] reported five patients, all successfully operated upon between the first and six and one-half months of pregnancy. He advocates interruption of mitral stenosis when the mother is classified as group 3 or 4. Watt [11] came to similar conclusions based on seven patients operated on without maternal death. Hall [12] emphasized the importance of an associated strict medical program and recommended surgery only as an adjunct to such a regimen. Mendelson [13] has reported 17 instances of mitral valvuloplasty during pregnancy without maternal death. His attitudes are strikingly similar to our own, in that a place exists for medical therapy, therapeutic abortion, and surgical intervention.

Direct surgical correction of mitral stenosis always embraces far more than the technical maneuver. This is particularly true when the associated alteration of physiological and hemodynamic mechanisms in pregnancy are added. Such a program involves proper selection of patients, meticulous care before and after surgery, as well as enlightened operative management. Failure to appreciate these cardinal precepts accounts for two of our three deaths.

We have previously emphasized the responsibility of the physician in the selection of patients with mitral stenosis for surgical treatment.[14a] When no complicating problem of pregnancy exists, as a guide we have used a classification[14b] based on symptoms and physical findings which has proved of value in preoperative evaluation and estimation of operative risk. Patients have been divided into four groups: 1, benign (murmur without handicap); 2, handicapped (disability without progression); 3, hazardous (progressively disabled); and 4, terminal (refractory failure in cardiac invalids). We have reserved surgery chiefly for patients in groups 3 and 4. The operative mortality in the absence of pregnancy is 0.6% in group 3, but rises to 20% when patients progress to group 4.[15]

Signs and symptoms attributable to the pregnancy per se must be borne in mind when considering the need for correcting mitral stenosis. For example, a functional systolic murmur appears in 50 to 70% of women during pregnancy. Thus, observations by competent clinicians before the onset of pregnancy are of great value. Almost invariably the heart rate increases and some shortness of breath develops. Changes in the cardiac silhouette may occur. The transverse position of the heart may give an erroneous impression of an increase in diameter. The usual lordotic posture of the pregnant woman may throw the pulmonary conus into relief and suggest enlargement.

Slight roughening of the mitral valve may in the presence of increased blood volume and blood flow produce a diastolic rumble, although there may be no significant stenosis. If this misleading murmur coincides with a progression of dyspnea due to causes other than valvular obstruction, e. g., rheumatic carditis, anemia, or overemphasis of physiological dyspnea, a false conclusion may be reached.

In short, we are reluctant to make the diagnosis of mitral stenosis *de novo* during pregnancy. The evaluation of a competent cardiologist before pregnancy concerning murmurs and clinical classifications is invaluable.

Operative Experience

Mitral valvuloplasty during pregnancy has been performed on 27 patients. Their ages varied from 19 to 36 years. Sixteen of these patients were in their third month of pregnancy. The remaining were from two and one-half to six months pregnant. One patient was classified as group 2, 25 as group 3, and one as group 4.

Twenty-four patients have survived and of these 23 are moderately to markedly improved. Twenty pregnancies proceeded to term. Twenty children,

including one set of twins, were born by pelvic delivery; one living child was born by cesarean section, elected because of a breech presentation. At the time of writing, the last patient in this group had progressed through her eighth month of pregnancy without event since valvuloplasty.

There have been three maternal deaths. The first occurred 33 days after the operation and was due to a cerebral embolus. The second died suddenly 18 hours after ventricular fibrillation had been successfully controlled by electric shock in the operating room. The last death followed interruption of a twin pregnancy, advised because of congestive heart failure complicating mitral insufficiency.

These maternal deaths accounted for one-half of the fetal deaths. Three other unsuccessful pregnancies were due to elective interruption because

Data on Twenty-seven Patients with Mitral Stenosis in Whom Valvuloplasty Was Carried Out During Pregnancy

No. of Case	Age of Patient	Previous Pregnancies No.	Signs and Symptoms Prior to Present Pregnancy* Symptoms						Physical Findings		Preoperative; Mo. of Pregnancy; Degree of MS†; Additional Findings	Operative Diagnosis and Valve Size, Sq. Cm.‡	Complications	Current Status	Fetal Status; Type of Delivery	Subsequent Pregnancies; Status of Child
			D	PND	PE	CHF	H		Rales	Liver	Edema					
1	26	2	+	+	+	0	+	+	0	+	+	3;3	MS;0.8	0	Active	Living; breech presentation; section	One section; died 24 hr.; one spontaneous abortion; one section, living and well
2	35	4	+	+	0	+	+	+	0	+	0	6;3	MS;0.8	0	Active	Living; NFTSD§	One spontaneous abortion; one NFTSD
3	30	4	+	+	0	0	0	0	0	+	0	3½;3;MI¶	MI;3.5	CHF	Limited; requires medical regimen	Nonviable at time of hysterotomy	0
4	33	3	+	+	+	+		+	0	0	0	3;3	MS;—1.0	0	Active	Living; NFTSD	0
5	19	0	0	+	+	+	+	+	0	0	0	4½;3	MS;0.8	0	Active	Living; NFTSD	One NFTSD One section
6	36	3	+	+	+	+	+	+	0	0	0	4½;3	MS;—1.0	0	Active	Living; NFTSD	0
7	28	2	+	+	+	+	+	+	0	0	0	3;3;¶MI	MS;1.0	Hypoxia; ventricular fibrillation	Dead; resuscitated in O.R.; ventricular fibrillation & death, 18 hr. p.o.	Dead	
8	23	1	+	+	+	0	0	0	0	0	+	2½;3	MS & MI; 1.3	0	Active	Living; NFTSD	One NFTSD
9	30	3	+	+	+	+	+	0	+	+	0	2½;3	MS;—1.0	0	Active	Dead; placenta previa—2 mo.	One spontaneous abortion
10	35	2	+	+	0	0	0	0	0	0	0	3;3	MS;—1.0	0	Active	Living; NFTSD	0
11	32	7	+	+	+	+	+	0	0	+	0	3;3; residual previous cerebral embolus	MS;—1.0	CVA	Dead 33 days p.o.; CHF—head not examined	Dead; spontaneous abortion 3 wk. postvalvuloplasty	0
12	28	0	0	+	+	+	0	+	+	+	+	3;3	MS;—1.0	0	Active	Living; NFTSD	One NFTSD
13	30	2	+	+	+	+	+	+	+	+	0	5½;3	MS & MI; —1.0	0	Active	Dead, 48 hr.; congenital heart disease	0
14	28	3	+	+	+	+	+	+	+	+	0	4½;4; twin pregnancy	MI;2.0	CHF	Dead one month p.o.—CHF, rheumatic carditis, MI	Dead after hysterotomy	
15	30	4	+	+	+	+	+	0	0	+	0	3½;3	MS;—1.0	0	Active	Living; NFTSD	Undelivered
16	26	0	0	+	+	0	+	+	0	0	0	2½;3	MS;1.5	0	Active	Living; NFTSD	0
17	29	4	+	+	+	+	0	+	0	0	0	3;3; twin pregnancy	MS;—1.0	0	Active	Twins living; NFTSD	0
18	32	3	+	+	0	+	0	+	0	0	0	3;3	MS;2.0	0	Active	Living; NFTSD	1 Undelivered
19	24	3	+	+	+	+	0	+	0	0	0	3;3	MS;—1.0	0	Active	Living; NFTSD	0
20	29	7	+	+	+	0	0	+	0	0	0	3;3	Reoperation; MS;1.2	0	Active	Living; NFTSD	0
21	33	3	0	+	+	0	+	0	0	0	0	3;3	MS;—1.0	0	Active	Living; NFTSD	0
22	31	1	+	+	0	+	0	0	+	0	0	3;?;A‖	MS,MI,& AI;1.3	0	Active	Living; NFTSD	0
23	27	0	0	+	+	+	0	0	0	+	0	3½;3	MS;—1.0	0	Active	Living; NFTSD	0
24	29	1	+	0	+	0	0	0	+	0	+	4;3	MS;—1.0	0	Active	Living; NFTSD	0
25	30	1	+	+	+	+	+	0	0	0	0	5;3	MS;—1.0	0	Active	Living; NFTSD	0
26	30	0	0	+	+	+	+	0	0	+	0	3;3	MS;—1.0	0	Active	Living; NFTSD	0
27	26	2	+	+	0	0	+	+	0	0	0	2½;3;A‖	MS & AI; —1.0	0	Pregnant	Due July, 1957‡	

* D=dyspnea; PND= paroxysmal nocturnal dyspnea; PE=pulmonary edema; CHF=congestive heart failure; H= hemoptysis.
† MS=mitral stenosis; and digit refers to group (see American Heart Association classification in text).
‡ Minus sign refers to orifice size less than indicated value.
§ MI=mitral insufficiency.
‖ AI= aortic insufficiency.
¶ NFTSD=normal full-term spontaneous delivery.
‡ Addendum: delivered uneventfully at term.

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of congestive failure and mitral insufficiency, placenta previa, and congenital heart disease. Details of all patients are presented in the table.

Comment

The place for surgical correction of mitral stenosis in pregnancy should be determined by the severity of the stenosis and the risk and quality of the available surgery. Unfortunately, the seriousness of mitral stenosis in pregnancy is at times as much confused as clarified by scrutiny. The more carefully cardiologists screen pregnant patients prior to delivery, the more auscultatory stenosis is added statistically to hemodynamically significant stenosis. This may have a tendency to give the illusion of safety for the "cardiac in pregnancy." Conversely, a lack of careful observation of nonpregnant women carelessly allows persons with group 2 and 3 mitral stenosis to go unrecognized until they are in serious difficulty, perhaps late in pregnancy. By this time either interruption of pregnancy or valvuloplasty may be hazardous, and a program of nonintervention may be lethal to the mother or child. The dividends available from a preventive program compromising correction of stenosis before pregnancy or the prevention of pregnancy cannot be overemphasized, although this maxim affords cold comfort to the physician dealing with the pregnant cardiac.

Causes of Three Maternal Deaths.—To determine the safety of valvuloplasty during pregnancy, not only do we need to know that 27 valvuloplasties were performed with 24 maternal survivals but we need to look carefuily at the 3 deaths. The first was in a patient in whom the diagnosis of mitral stenosis had not been established before gestation. The pitfall of diagnosing stenosis primarily from murmurs was not appreciated. Mitral insufficiency was found at operation and not relieved. Congestive failure progressed, and interruption of the twin pregnancy was undertaken 23 days after valvuloplasty. The patient subsequently died. The relative parts played by digitalis intoxication, electrolyte imbalance, rheumatic activity, and congestive heart failure from regurgitation cannot be fully assessed. Perhaps catheterization of the left side of the heart would have avoided this error in diagnosis.

The second death was incident to a cerebral embolus. This patient, who had embolized preoperatively, sustained another embolus the day after valvuloplasty and died one month later. Cerebral embolization after mitral valvuloplasty has approached an irreducible minimum (2% in group 2 and 3 and 9% in group 4), but will always constitute a threat in this operation. Its occurrence in this individual can hardly be related to the pregnant state.

The third death was in a patient with associated aortic disease who developed ventricular fibrillation during operation. She was successfully defibrillated but died suddenly 18 hours later. Perhaps current improved anesthetic and surgical techniques would have avoided this. There is no clear causal connection with the pregnancy.

Causes of Three Additional Fetal Deaths.—In addition to the fetal deaths associated with the above maternal losses, there were three others. In one of these the pregnancy was interrupted by hysterotomy because the patient did poorly after valvuloplasty. She has survived but is unimproved because of associated mitral insufficiency. The second fetal loss with maternal survival was incident to a placenta previa during the seventh month of pregnancy. The third infant death occurred 48 hours after delivery and was due to congenital heart disease. This is the only proved occurrence of a congenital defect in an infant in the series. The valvuloplasty was performed in the sixth month of pregnancy, and the mother has since done well. The remaining children delivered after mitral valvuloplasty in pregnancy are living and well.

Further Pregnancies and Rehabilitation of 24 Survivors.—A word should be added about further pregnancies and rehabilitation of the 24 survivors. Twenty-three of the original 27 are markedly or moderately improved. The only unimproved patient is suffering from severe mitral insufficiency, as mentioned above. The error in the preoperative diagnosis of this case might now be avoided by catheterization of the left side of the heart. There have been 12 subsequent pregnancies in eight of these patients. Six normal children have been born and two women have not delivered at the time of writing. Four were pelvic deliveries and two were by section. Three pregnancies ended in spontaneous abortion, and one infant died after delivery by cesarean section. This experience emphasizes that routine sterilization in these patients is not justified.

In the larger series of 1,000 valvuloplasties on nonpregnant patients there have been 34 successful subsequent pregnancies, including one live triplet birth.[16] The evidence that properly conducted cardiac surgery for mitral stenosis in pregnant patients is inordinately hazardous would seem to be lacking.

Total Care.—The concept of total care in managing a patient through valvular surgery has received consideration in previous publications.[17] It includes (1) preoperative digitalis regulation, salt-restriction, correction of electrolyte imbalance, and appropriate diuresis, (2) expeditious surgery, (3) meticulous anesthetic technique, minimal use of anesthetic agent, maximal ventilation, oxygenation, and the avoidance of tachycardia and hypotension, and (4) careful postoperative supervision, maintenance of oxygenation, and prompt reinstitution of a full cardiac regimen.

Pregnancy brings this need for total care into more urgent focus and presents at least a few specific problems. The end of the first trimester seems

a satisfactory time for valvuloplasty. The pregnancy is secure yet the burden of gestation relatively low. It is presumed that periods of anoxia should be avoided lest the incidence of congenital anomalies increase. The same conservatism that prompts the full medical regimen directs us to stress rest virtually to the point of invalidism during the periods of peak burden (32d to 36th week and the first postpartum week). Finally, it must be emphasized that cesarean section increases rather than reduces the burden of delivery, unless pelvic delivery is specifically contraindicated. If cesarean section is carried out at the end of the eighth month when the work load of pregnancy is at its peak, the felony is compounded.

Surgical Management Indicated When Baby Desperately Wanted.—In conclusion, one significant indication for correcting the mitral stenosis with salvage of pregnancy involves the fact that many people simply want babies. When we speculate as to how much of a risk is justified, the problem becomes both individual and philosophical. A review of the facts indicates that in properly selected patients who are not pregnant the risk of valvuloplasty for mitral stenosis is low (group 3, 0.6%) and there is little evidence that pregnancy renders this risk more formidable. A single illustrative case history is in order.

CASE 18.—A young matron had had progressive dyspnea on exertion. She had seen Dr. Laurence B. Ellis within the previous year. Mitral stenosis was diagnosed and valvuloplasty recommended. She and her husband desperately wanted children but she had miscarried by the sixth month in four previous pregnancies. Before surgery could be arranged she was well into the first trimester of another pregnancy and in refractory pulmonary congestion. Immediate valvuloplasty was favored by Ellis and by us. Other conscientious "conservative" opinion convinced the patient that pregnancy should be interrupted and that she should have valvuloplasty with the view to subsequent pregnancy. The patient became deeply disturbed emotionally just before the abortion and insisted on "trying just once more to go through pregnancy"—this time having her stenosis corrected before she again miscarried. Valvuloplasty was carried out quickly and effectively at the end of the third month. Pregnancy proceeded uneventfully and at term she spontaneously delivered a fine pair of twins.

Summary

The additive effect of mitral stenosis and the usual hemodynamic alterations occurring in pregnancy produces a therapeutic problem of considerable complexity and importance. The physician confronted with this problem must consider the merits of three alternative methods of management: medical therapy, therapeutic abortion, and "total surgical management."

Valvuloplasty was carried out in 27 pregnant women with mitral stenosis. There were three maternal deaths. Two were believed to be unrelated to the associated pregnancy. Twenty healthy children have resulted. Twenty-three of the mothers are moderately to markedly improved over their prepregnant status.

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CHEMOTHERAPY OF DEPRESSION

USE OF MEPROBAMATE COMBINED WITH BENACTYZINE (2-DIETHYLAMINOETHYL BENZILATE) HYDROCHLORIDE

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Depression, defined as a state of sadness, with self-reproaches, psychomotor inhibition, sleep disturbance, and impaired appetite, was treated in 35 consecutive patients by the simultaneous use of meprobamate and benactyzine hydrochloride. The meprobamate was given initially in doses of 400 mg. four times daily and, when necessary, gradually increased to 1,200 mg. four times daily; its purpose was to relax and reduce excitability without exerting a significant inhibitory effect. The benactyzine was given initially in doses of 1 mg. four times daily and, when necessary, gradually increased to 3 mg. four times daily; it is a mild anti-depressant particularly effective in relieving the ruminative obsessive aspects of the depressive mood. Close supervision extending over the entire 24-hour span of each day had to be assured because of the risk of suicide. The usual supportive psychotherapy was given concurrently. Three case histories illustrate the procedure. The average duration of treatment was eight weeks, and 20 patients (57%) made a complete and/or social recovery. This is higher than the rate of spontaneous recovery under comparable conditions. It is not as high as the rate of recoveries obtained by electroshock therapy. This treatment is therefore recommended as an initial step in the treatment of depressions, designed to reduce the number of patients requiring electroshock therapy.

The chemotherapeutic agents available for treatment of mental illness today are best adapted to the treatment of states of excitation, with panic and anxiety, and especially mania. Their effect is achieved by inhibition of primary subcortical epinephrine-precipitable anxiety,[1] probably by exerting a selective inhibitory effect upon the posterior hypothalamus.[2] In the conditioned reflex experiment, they are shown to inhibit the orienting response but to have no effect on the learned responses such as well-established conditioned reflexes.[3] In remarkable conformity with this model, they extinguish the unconditioned excitatory psychotic disorganization of the higher cortical activity (panic or mania), which probably has its origin in the upsurge of anxiety from the subcortical emotional centers, but do not extinguish the deeply ingrained learned responses that underlie neurotic behavior. Although early enthusiasts reporting the use of the new tranquilizing drugs had claimed that these drugs also relieved depressions, it soon emerged that true depressions not only are not relieved by chlorpromazine and reserpine but are aggravated by these tranquilizing drugs.[4] Denber [5] has recently reinvestigated this problem. The discharge rate he obtained, 15 out of 45 patients (33%), is less than the spontaneous recovery rate for depressions. This appears to confirm the clinical experience of others, namely, that chlorpromazine inhibits rather than aids recovery from depression. Recently, Denber [6] treated 10 patients on a regimen of 100 mg. of chlorpromazine and 500 mg. of diethazine three times daily to the point of marked disorganization of the cerebral electroactivity, and he reported marked alleviation of the depressive state. However, this treatment is still experimental and should be administered only under conditions of hospitalization.

In this connection it is important to define depression as a state of sadness with self-reproaches and psychomotor inhibition, with sleep disturbance (difficulty in falling asleep, frequent waking at night, and early waking in the morning), and with disturbance of appetite. Certain reactive depressions, in which retardation and turning against the self in a hostile manner are absent, reveal themselves not only psychologically and clinically but also physiologically, as demonstrated by testing by means of the epinephrine (Adrenalin)–methacholine (Mecholyl) chloride and sedation threshold tests,[7] to be anxiety states with discouragement rather than true depressions, and these indeed respond to tranquilizing drug therapy, in contradistinction to the true depressive states.[8]

Excitatory drugs have on the whole remained ineffective in severe depressive states. This was the case with amphetamine (Benzedrine) sulfate and its derivatives, including dextro amphetamine (Dexedrine) sulfate and methamphetamine (Pervitin) hydrochloride, and some newer drugs such as pipradrol (Meratran) hydrochloride, isoniazid, and SKF-5 [2-amino-1-(3,4-methylene-dioxyphenyl) propane hydrochloride], which others as well as myself have had occasion to subject to experiment-

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al trial in recent years. Unfortunately, these drugs, in my experience, often make severely depressed patients more disturbed, in that they increase the charge of emotional energy and thus potentiate tension; this occurs even in therapy with such excitatory drugs as dextro amphetamine, which has a euphoriant effect that pipradrol and SKF-5 lack. The combination of such drugs with amobarbital sodium (sodium Amytal) has been more easily tolerated by these patients but has not made the treatment more effective. Furthermore, whenever these stimulatory drugs are used, treatment with these drugs has to be supplemented by fairly heavy doses of hypnotics at night, which tend to deepen the depression on the following morning. In some of the recent series reporting the use of stimulatory and other drugs, patients with inert states of lessened zest incidental to chronic schizophrenia have been studied [9] or included among those treated.[10] With or without the inclusion of such cases, the effect of stimulatory medication, as well as the results of other stimulatory techniques, has been disappointing in the treatment of depression; the recovery rates reported tend to fall short of the spontaneous recovery rates. Recently, Kline and co-workers [11] introduced a new stimulant, namely, iproniazid (Marsilid), administering 50 mg. by mouth three times daily. Iproniazid has a stimulating and energizing effect by virtue of the fact that it inhibits the enzymes which destroy catecholamines (epinephrine, norepinephrine, and allied substances). The fact that epinephrine may relieve depression temporarily had been observed before.[8] In view of the fact that the energizing effect of iproniazid is not associated with a significant euphoriant effect, the addition of dextro amphetamine (5 mg. twice daily) is recommended in order to render the mood cheerful, and nocturnal hypnotics are necessary in order to produce sleep. Vitamin B_6 (50 mg. daily) has to be added to protect against side-effects.

In connection with the problem of evaluation of treatment, it is important to remember that all drug therapy available in psychiatry today does not significantly increase the rate of complete and/or social recovery but merely allows it to materialize earlier or after less harassing morbidity. Only lesser grades of improvement ensue at a greater rate than obtained spontaneously. The drug "covers" the psychosis as it were, compensating for it. Therefore, the most effective use of these drugs is in the self-limited psychoses such as mania or the naturally short-lived schizoaffective psychoses. It is, of course, quite possible that drugs will be discovered that will improve upon the spontaneous rate of complete and/or social recovery.

The rate for spontaneous recovery (complete and/or social) from depression is 66.4% (of 116 cases), with recovery occurring during the first year of the illness in only 44%. This rate is not improved upon by intensive psychotherapy; it was 46.6% for 208 patients so treated. The complete and/or social recovery rate for depressed patients treated with electroshock therapy is 67.9% within the first year (of 2,165 cases reported).[12] It was 73% in a smaller series of my own (76 consecutive cases).

Requirements for Chemotherapy of Depression

On the basis of our experience with the use of electroshock, which so far has been the best treatment available for depression, a drug or combination of drugs useful for the relief, control, or reversal of depression would have to fulfill the following two requirements: it would have to reduce the excitability of the higher cortical substratums of the ego without inhibiting the subcortical hypothalamic centers; and it would have to strengthen the ego boundaries and defenses (Rado's [13] pain barrier). Such a chemotherapeutic agent should be able to counteract the depressive state in the same effective manner as tranquilizing drug therapy counteracts the manic state, allowing the patient a significant measure of normal functioning until recovery supervenes. Among such effects of lessened morbidity should be a restoration of the normal sleep pattern without the added use of hypnotic medication. The ultimate recovery rate in a sufficiently large series of cases should be equal to or better than the spontaneous recovery rate.

There is no single drug that could fulfill the two basic requirements mentioned above. However, there is one drug which fulfills the first requirement, namely meprobamate (Miltown), which relaxes and reduces excitability without exerting a significant inhibitory effect,[14] and another drug which fulfills the second, namely, benactyzine (2-diethylaminoethyl benzilate) hydrochloride, which strengthens the ego boundaries and thus reduces the psychic pain, fear, and resulting inhibitory avoidance responses engendered by stress.[15]

The manner in which meprobamate accomplishes its selective reduction of excitability—in terms of the conditioned reflex technique—is not known. It is known, however, that benactyzine facilitates the orienting response and the formation of new conditioned reflexes, thus counteracting the inhibitory state of the higher cortical activity. In remarkable accord with this conceptual scheme, benactyzine has proved itself to be mildly antidepressant and particularly effective in relieving the ruminative obsessive aspects of the depressive mood.[16] However, it failed to relieve the sleep disturbance of the depressed patient and often brought to the fore anxious tension. The antidepressant effect of this drug appears to be thus due to strengthening of the ego boundaries rather than to diminution of excitability. Meprobamate, on the other hand, has no recognizable or significant antidepressant effect but appears capable of reducing excitability without producing inhibitory states. Furthermore, Berger [14] had already observed that meprobamate while not a hypnotic, tended to restore the normal sleep pattern. It appeared promising, therefore, to combine these two drugs and to determine

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whether this drug combination proved capable of reversing the symptomatology of the depressed patient, especially his sad affect, his hostile turning against himself, and the disturbance of his sleep pattern, and whether it proved capable, and to what degree unaided by other measures, of producing a complete and/or social recovery rate during the first year of illness equal to or better than the spontaneous recovery rate.

Clinical Study

This study was carried out in 35 consecutive patients who suffered from depression sufficiently severe to warrant the consideration of physical treatment methods. The tablets used contained either 200 mg. of meprobamate and 0.5 mg. of benactyzine or 400 mg. of meprobamate and 1 mg. of benactyzine. The initial dosage was usually 400 mg. of meprobamate and 1 mg. of benactyzine four times daily, the smaller single dose having been found ineffective as an initial dosage. If then necessary, the dosage was gradually increased up to 1,200 mg. of meprobamate and 3 mg. of benactyzine, four times daily. The risk of the patients' committing suicide involved in this type of treatment was given due consideration, and 24-hour supervision at home was arranged and preliminary arrangements were made for immediate hospitalization upon the first indications of an active suicidal trend.

The duration of treatment in the cases presented here varied from two weeks to six months. No serious side-effects were encountered (no skin rashes, no gastrointestinal disturbances or disturbances of the hematopoietic system). Of the 35 depressed patients in this series, only 5 complained of subjective side-effects. One patient, a 27-year-old male, complained of throbbing sensations when taking large doses of the medicaments (800 mg. of meprobamate and 2 mg. or benactyzine) closer together than prescribed (i. e., less than four hours apart). This is to be ascribed to benactyzine, since it did not occur with meprobamate alone nor did it occur with smaller doses (400 mg. of meprobamate and 1 mg. of benactyzine). A female patient, aged 32, complained of prickly paresthesias and causalgic sensitivity of the left thumb when on a regimen of 400 mg. of meprobamate and 1 mg. of benactyzine four times daily. This effect subsided when the benactyzine therapy was discontinued. Another patient, a 70-year-old woman, complained of vertigo and stupor reminiscent of alcoholic intoxication when the dosage was increased to 800 mg. of meprobamate and 2 mg. of benactyzine four times daily. This condition was remedied promptly by reduction of the dosage by half.

A depressed female patient, aged 39, complained of "overexcitement" which subsided after discontinuing use of benactyzine; and a 72-year-old woman reported dryness of the mouth while she was on benactyzine therapy. It was of particular interest that drowsiness was complained of very rarely and could be promptly and effectively controlled within a day or two by lowering of the dosage. As improvement supervened, the dosage was gradually reduced to below the minimum initial dosage and then gradually tapered off by reducing the number of daily doses. The usual supportive psychotherapy, including clarification of traumatic issues, was administered concurrently. The management of patients may be best illustrated by a few brief case reports.

Report of Cases

Case 1.—A 48-year-old woman who had a previous episode of depression 14 years ago came to treatment four months after the onset of a severe depression. Her illness manifested itself with disconsolate sadness, self-reproaches, suicidal thoughts, sleep disturbance, and gastric somatization reaction with loss of appetite and loss of 15 lb. (6.8 kg.) in weight. She was unable to do her housework or enjoy any of her usual social activities. The epinephrine-methacholine test showed a type 6 response with absence of epinephrine-precipitable anxiety. A regimen of 400 mg. of meprobamate and 1 mg. of benactyzine four times daily (no nocturnal hynotics were prescribed) produced marked improvement within four days. One week later, the patient reported that she was much better. However, self-castigation was still evident, and therefore the dosage was increased to 800 mg. of meprobamate and 2 mg. of benactyzine four times daily. Two weeks later, the patient reported that she was feeling quite well and sleeping well for seven to nine hours per night. However, her husband stated that occasionally she still brought up suicidal thoughts; therefore, the dose was reduced to 400 mg. of meprobamate and 1 mg. of benactyzine four times daily, since it was felt that at this time, in her otherwise improved state, her defenses might reassert themselves more effectively if the daytime relaxation were reduced. Eleven weeks after the beginning of treatment, the patient considered herself "95% recovered." She was doing all her own work and engaging in all her social activities. Her only remaining complaint was a little tightening in the throat and "tenderness of the head." By the 13th week, with improvement proceeding apace, reduction of the dosage was begun. Full recovery, without residual complaints, was established 16 weeks after the beginning of treatment. Medication was discontinued one week later. The patient's complete recovery has remained sustained.

Case 2.—Another case in point is that of a 40-year-old male suffering from a depression of one and one-half years' duration in which sleep disturbance was particularly prominent. For seven months preceding treatment, he had stepped up the dose of barbiturates to 6 grains (0.39 Gm.) of secobarbital (Seconal) or 9 grains (0.58 Gm.) of amobarbital, respectively, without being able to obtain a full night's sleep even with such large doses of hypnotics. On a regimen of 400 mg. of meprobamate and 1 mg. of benactyzine morning and noon and 800 mg. of meprobamate and 2 mg. of benactyzine afternoon and evening, the patient improved steadily, being able to omit nocturnal hypnotic medication entirely after 19 days of treatment (dosage having been gradually reduced up to that time). Restoration of normal sleep pattern was complete after 40 days of treatment. Full recovery was achieved one month later, eight weeks after the beginning of treatment.

Case 3.—Of particular interest is the case of a 59-year-old male patient who was suffering from an involutional agitated depression of one month's duration when treatment began. Four hundred milligrams of meprobamate and 1 mg. of benactyzine four times daily were prescribed, and the patient appeared to improve for the first few days but then started to relapse. Therefore, the dose was increased after one week to 800 mg. of meprobamate and 2 mg. of benactyzine four times daily. On this regimen the improvement was still slow, and therefore the dose was increased to 1,200

mg. of meprobamate and 3 mg. of benactyzine four times daily on the 20th day of treatment. Nineteen days later, significant improvement came to the fore. The patient was able to relax and stated that he felt quite well though not yet up to par. One month later, there was enough improvement so that the dose could be gradually reduced; nevertheless, the patient did not achieve a state of social recovery until after 25 weeks of treatment. This state, however, bordered closely on complete recovery, with only minor insignificant complaints remaining. It should be emphasized that from the sixth week on (the 39th treatment day), this patient was practically convalescent and the harassing aspects of his illness had disappeared. This patient is of particular interest because he had suffered a previous attack of depression for which I had treated him with electroshock. Twenty-one electroshock treatments were administered during the first 50 days of that illness, and subsequently the patient entered a convalescent phase which extended (including the treatment period itself) over a period of 44 weeks, when social recovery bordering on full recovery supervened. In retrospect, one may say that neither treatment brought about the recovery of this patient but that the treatment merely mitigated the manifestations of illness until spontaneous recovery asserted itself. As a means of covering the symptoms and managing the patient, the drug regimen was certainly less strenuous for the patient and his family than the previous course of electroshock therapy in this particular case.

Results

Twenty of the 35 patients in a state of depression who were treated achieved a state of complete and/or social recovery within 1 to 25 weeks, the average being 8 weeks. Twenty-six of these patients had psychotic depressions of the manic-depressive or involutional type, while nine had neurotic depressions. The age of the patients with psychotic depressions varied from 27 to 70 years, the average being 49 years; that of patients with neurotic depressions varied from 32 to 72 years, the average being 44 years. The duration of the psychotic depressions varied from 2 weeks to 2 years, the average being 13 months; that of the neurotic depressions varied from 1 month to 2 years, the average being 9 months. It is of interest to find that the recovery rate for these two groups is identical. Fifteen of the psychotics recovered, making a recovery rate of 58%, while five of the neurotics recovered, making a recovery rate of 55%. The recovery rate for the total group was 57%. The duration of treatment until recovery supervened was likewise almost identical. It varied from 1 to 25 weeks for psychotic depression and from 2 to 23 weeks for neurotic depression, the average being 8 weeks for both groups.

In the 20 patients responding favorably, the early effect of the new drug combination was a marked reduction of tension and depressive rumination as well as a striking reduction in hostility toward the self and of suicidal trends. Resumption of the normal sleep rhythm was also one of the striking early effects. It was possible to discontinue the nocturnal use of hypnotics, in the patients who had started using them before treatment began, before eventual recovery supervened. None of these 20 patients had to be hospitalized, and none of them made suicide attempts.

Of the 15 patients who did not respond within two to six weeks, 9 were treated with electroshock therapy (5 as outpatients and 4 under conditions of hospitalization), and 8 of them achieved recovery. Three others were given other drugs, and one patient (with chronic depression) was subjected to intensive psychotherapy unaided by physical measures. One other patient with chronic illness underwent a lobotomy, since electroshock and other treatments had failed in the past. One patient was still, at the time of writing, on the meprobamate-benactyzine regimen after nine weeks; although he is listed in this study as not recovered, he was sufficiently improved for part-time work. Interestingly enough, none of the patients in the group who did not recover attempted suicide even while on the meprobamate-benactyzine regimen.

The recovery of 20 of 35 patients is highly promising, as it represents a recovery rate of 57%, which is definitely in excess of the spontaneous recovery rate expected during the first year of illness and remains only slightly below the recovery rate obtainable with electroshock therapy. The total number of cases, of course, is as yet too small to establish this rate as significant. However, the alleviation of specific and crucial symptoms, even in those patients who failed to achieve complete and/or social recovery and had to be subjected to electroshock ultimately, renders further work with this drug combination desirable and promising.

Summary and Conclusions

With treatment of depression by the combined use of meprobamate and benactyzine (2-diethylaminoethyl benzilate) hydrochloride, complete and/or social recovery of 20 of the 35 patients treated (57%) supervened within 1 to 25 weeks, the average being 8 weeks. Side-effects were minimal and easily controlled. Patients who did not show some favorable response within two weeks and/or marked improvement within six weeks were treated by other means, including electroshock.

Treatment of depressions by drugs is contingent upon arrangements (either at home or in hospital) to protect the patient from the risk of suicide. The use of meprobamate-benactyzine treatment for depression is recommended as a step which allows those patients to recover for whom this treatment is sufficient, thus screening out and reducing the number of patients requiring electroshock therapy.

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The meprobamate and the benactyzine hydrochloride (Deprol) used in this study were supplied by Wallace Laboratories, New Brunswick, N. J.

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RECONSTRUCTIVE SURGERY FOR HYDRONEPHROSIS

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Reconstructive surgery about the renal pelvis in the past has been assumed to call for the use of splinting catheters and nephrostomy tubes. Recent experience has convinced the authors that better results are obtained without these aids provided certain principles are followed. The kidney should be completely mobilized and the ureteropelvic juncture exposed for inspection. Nephropexy is done to elevate the kidney and hold the ureter in a straight line. The continuity of the pelvic and ureteral wall should be preserved, for transection is followed by weeks of dysfunction. Excessive stitching is avoided, and no attempt is made to obtain a watertight closure. Rubber drains extending down to the renal pelvis are left in the abdomen for at least nine days. Eleven patients treated surgically in this way were able to leave the hospital on or before the 14th day in every case. One patient with a long history of lithiasis had recurrences that finally necessitated nephrectomy. The others showed steady improvement after operation with respect to both the function and the appearance of the renal pelvis.

Over five years have passed since splinting catheters and nephrostomy tubes have been eliminated in reconstructive operations on the renal pelvis. The results have been such that this principle is to be continued. Splinting tubes have enjoyed wide usage in the past, and many good results have been attributed to them. I do not propose that their elimination will bring perfect results in every instance. All reconstructive or plastic procedures are fraught with a certain element of failure. Our experience indicates, however, that just as good and perhaps better results are obtained without their use. Also the technique of the operation is greatly simplified and shortened and the period of hospitalization is only one-half to one-third as long, as most surgeons using splints recommend that they remain in the kidney during the postoperative period for four to six weeks—and even longer periods have been mentioned at times. Weaver [1] states that six weeks is required for complete regeneration of the ureter. More specifically, there are four objections to the splints.

1. There is possibility of infection. When a tube or catheter extends from the epithelium of the kidney or ureter to the exterior, the epithelium

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must be regarded as being exposed to the external environment. Mixed infections, including those resulting from drug-resistant organisms, frequently result. Henline [2] reported an incidence of stone formation in 11% of 45 patients in whom splints were used in reconstructive surgery.

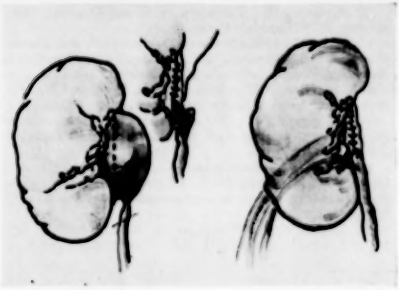

Fig. 1.—Type of reconstructive operation that has not given good results. Continuity of ureter and renal pelvis should be preserved if possible.

2. Stricture formation may occur not only at the operative site but in the ureter at the level of the end of the splint. Those using splints are not in agreement concerning the size of the splint. Davis [3] recommends a large caliber splint and states that after regeneration the lumen of the ureter will be even larger than normal after its use, whereas Weaver [4] from his experimental work on dogs found that a large diameter splint results in fibrosis and stricture formation and that a small caliber splint gives better results. Weinberg and I [5] have observed satisfactory regeneration of dogs' ureters, without any splinting, following linear excision of one-third to one-half of the ureteral wall for a distance of 3 cm. in 7 of 11 dogs.

3. Splinting tubes, when allowed to remain in the ureter for prolonged periods, may become occluded with incrustations and may produce obstruction.

4. Erosion through the ureter into the iliac vessels has been reported following the use of an indwelling ureteral catheter. Schoenemann [6] reported a fatal hemorrhage in a young female patient in whom an indwelling ureteral catheter had been present for six weeks while she was being treated for pyelonephritis of pregnancy.

Technique

The technique for correction of obstruction at the ureteropelvic juncture has been simplified by the elimination of these unnecessary adjuncts. At operation the kidney is completely mobilized and the ureteropelvic juncture is exposed; all possible external causes of obstruction are removed. Fibrous bands and anomalous vessels are not uncommon. If the vessels are small and supply only an insignificant part of the lower pole, they are divided and ligated. The small portion of the parenchyma supplied by them will undergo quiet atrophy and produce no trouble. If the vessels are of large size and if gentle occlusion with a rubber-shod clamp

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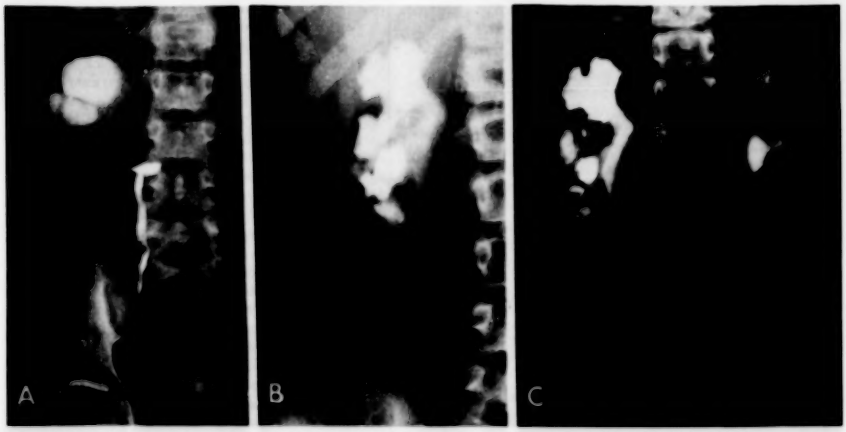

Fig. 2.—Continued recovery, over a two-year period, from hydronephrosis on the right. *A*, pyelogram in 7-year-old girl. Kidney estimated to contain over 200 cc. of infected urine. Catheter could not enter renal pelvis. *B*, pyelogram taken one year postoperatively. *C*, pyelogram taken two years postoperatively. Note funneling of ureteropelvic juncture in follow-up films. Urine is free of infection.

produces cyanosis in a major portion of the kidney, a serious attempt should be made to preserve the vessels. This may be done by changing the axis of the kidney or changing the course of the vessels by taking a few sutures through the tunica adventitia of the vessels, fastening them at a higher level on the pelvis, thereby relieving pressure at the ureteropelvic juncture.

The ureteropelvic juncture is opened routinely for inspection of the internal diameter, as calibration with a catheter through an opening in the pelvis is not reliable. If there is no evidence of internal obstruction, the incision into the renal pelvis and ureter is allowed to remain unsutured. A nephropexy is done to elevate the kidney and hold the ureter in a straight line. The wound is closed, and a rubber tissue drain is passed to the opening and allowed to remain for nine days. If intrinsic obstruction is found, a plastic procedure is done. The choice of technique depends on the type of obstruction found.

An operation that preserves the continuity of the pelvic and ureteral wall is preferred. Complete transverse section of the ureter followed by reimplantation into the pelvis has not given as good results as those procedures where continuity of the wall is maintained (fig. 1). A complete transection of the ureter interrupts synchronous peristalsis for several weeks, and dilatation of the proximal segment results.

Either the Schweizer-Foley type of Y-plasty or the flap operation advocated by Culp [7] have been used in this series. Both methods are excellent, and there are times when one is preferred over the other. The flap has several advantages; it can be cut from almost any part of the renal pelvis that is convenient. It can be made fairly long at times and used for repair of constricted areas that extend a moderate distance below the ureteropelvic juncture into the ureter. The flap should be provided with a broad base and a well-rounded end. These principles are essential in preserving adequate blood supply. Although the blood supply of the renal pelvis normally is extremely rich, the V-Y type of plastic operation provides a sharp point of tissue at the apex of the V which may be vulnerable to slough. At least skin will become necrotic when treated in this manner. A high insertion of the ureter is probably the prime indication for the V-Y type of operation.

Suturing of the flap is done carefully, using interrupted 00000 atraumatic sutures; excessive stitching produces fibrosis and is therefore to be avoided. No attempt is made to obtain a watertight closure. If there is any obstruction distal to the point of repair, a suture line will not hold anyway. The redundant renal pelvis is not resected unless its size is excessive. Hydronephrotic renal pelves will return to a size that will function normally if obstruction is completely removed. Unnecessary

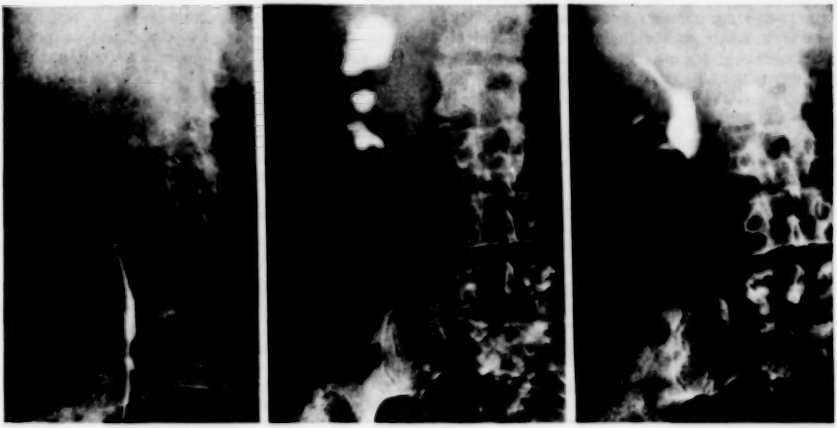

Fig. 3.—Urograms of patient, aged 52, admitted to hospital with anuria. Nephrectomy on the left had previously been was done. *B*, intravenous urogram taken 14 days after operation on ureteropelvic juncture. *C*, intravenous urogram taken two years postoperatively. Note good funneling at ureteropelvic juncture. Urine is free of infection.

cutting and stitching of the pelvic tissues should be avoided to keep fibrosis to a minimum. A nephrostomy tube is not used, as drainage is provided by leaving a vent 1.5 cm. long in the renal pelvis for egress of urine or blood clots. The repair may be carried out over a good-sized ureteral catheter, but this is removed as soon as the operation is completed, and no foreign body is allowed to remain in the kidney during the convalescent period.

The kidney is replaced high in its bed and secured in this position by a few interrupted sutures placed between Gerota's fascia and the fascia of the psoas, as described by Deming.[8] It is essential to keep the upper ureter in its normal bed and to prevent angulation, kinking, or an S-shaped deformity that sometimes results when the kidney resumes a lower position following mobilization. It is extremely important to maintain adequate drainage until the ureter is securely healed. The rubber tissue drains should be carefully placed down to the opening in the renal pelvis and not disturbed for a minimum of nine days. In our experimental work on dogs' ureters, fibrosis and stricture from urinary extravasation followed in all instances when the drain was removed before the ninth day.

In most of our patients surprisingly little urinary drainage resulted in spite of the fairly large opening in the renal pelvis. In the occasional instance when drainage persisted for 10 days, a cystoscope was introduced, and a ureteral catheter was passed up to the renal pelvis to dislodge a possible plug of mucus or blood clot; the catheter was then withdrawn.

Results

A total of 11 patients have been operated on with use of these techniques. All were discharged from the hospital on or before the 14th day. In none were secondary nephrectomy required because of failure of the anastomosis to function. In one patient, a woman who had formed soft stones of the "ground substance" variety for several years, a flap operation was done in 1954. She was free of infection and stones for several months; then the formation of soft stones resumed, and a nephrectomy was done 18 months later because of recurrent stones and infection. A good ureteropelvic juncture was found in the removed kidney. Poor results can be anticipated when reconstructive surgery is done on the pelves of kidneys that have formed stones repeatedly or in those that have been severely infected for long periods. The remaining 10 patients have enjoyed good results.

In appraising results the following criteria must be considered: 1. The kidney must be free of infection. 2. The ureter should drain the most dependent part of the pelvis. 3. Good funnel shape should be present at the ureteropelvic juncture. 4. The patient should be free of symptoms (pain).

Pain is probably the most difficult symptom to evaluate, as certain patients will have pain in the wound for months following any type of renal operation. If infection is absent and the kidney functions well and pyelograms show no evidence of obstruction, it can be assumed the pain will eventually disappear.

Patience and time are required for the renal pelvis to return to normal. In some instances (fig. 2 and 3) continued improvement has been observed in the appearance of the renal pelvis for over two years; there has been no infection and no pain. The functioning of the kidney has continued to improve.

Summary

Elimination of tubes and splints in reconstructive operations on the ureteropelvic juncture for the relief of obstruction can be done with gratifying results. Their elimination reduces postoperative renal infection and other foreign body reactions. The surgical technique is reduced to its simplest possible fundamentals, permitting shorter operating time. The convalescence period is greatly reduced.

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EFFICACY OF POLIOMYELITIS VACCINE

WITH SPECIAL REFERENCE TO ITS USE IN MINNESOTA IN 1955-1956

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A measure of the effectiveness of vaccination against poliomyelitis has been sought in the data from Minnesota, where the administration of Salk vaccine began in May, 1955. With the usual methods of comparison, utilizing trends in total and paralytic attack rates, the results have been difficult to interpret. The rate per 100,000 for all cases fell steadily from 131.6 in 1952 to 4.5 in 1956; but the fall began before vaccination, and the figure 4.5 is little lower than the 6.7 observed in 1947. Similarly the rate for paralytic cases fell steadily from 68.4 in 1952 to 2.1 in 1956; the fall began before vaccination, and the figure 2.1 is little lower than the minimum of 3.7 observed in 1947. The data for Minnesota are complete as regards the ratio of paralytic to total cases since 1946 and show a consistent trend downward from that year, the ratio of 46.2 for 1956 is little lower than that of 48.4 for 1954 and could be interpreted as continuing the trend. However, when a "life-table" method was applied to the data on poliomyelitis experience of vaccinated and unvaccinated groups, it indicated that two doses of the vaccine effected a significant reduction of the incidence of paralysis although single doses did not. It is concluded that Salk vaccine as utilized in Minnesota exerted a significant protective effect when two doses were given.

Prior to the application of the Salk poliomyelitis vaccine in 1954, in what may have been the largest field trial in history, sufficient concern as to its safety on the one hand and doubt as to its efficacy on the other existed in so many quarters as to engender serious question of the propriety of such a large scale application, at least until more nearly adequate tests of safety could be developed. Some investigators were of the opinion that only live virus vaccines could be efficient antigens and that a highly efficient vaccine might, therefore, contain live virus. Since Salk [1] was not working with attenuated strains but was rather applying formalin to demonstrably virulent strains of poliovirus and claiming complete killing, efficacy also remained in doubt.

On the other hand, a voluminous literature existed emphasizing the role which certain autarceologic, or innate, host factors might play in resistance irrespective of antibody level. Would vaccination in a recently tonsillectomized individual, or in a pregnant woman with temporarily altered hormonal balance, or in an individual recently inoculated with other antigens, protect against clinical poliomyelitis? Such possibilities of lowered resistance in individuals coupled with the fact that clinical poliomyelitis occurred but once for each 100 to 1,000 infections [2] made it abundantly clear that proof of efficacy of any poliomyelitis vaccine would ultimately have to be derived from field studies and that these would have to be a considerable size.

With the successful completion of the 1954 field trial and its demonstration of the reasonably high efficiency as well as the safety of the vaccines employed that year,[3] formalinized poliomyelitis vaccine was removed overnight from its experimental status and its use limited only by the difficulties of its mass production. Despite this development a few epidemiologists retained their concern for the continued safety and efficacy of the Salk vaccine and justifiably so. It was felt that continuing surveillance of all reported poliomyelitis cases, correlated with vaccinal history, was necessary to maintain vigilance on safety and effectiveness. Furthermore, changes in the procedures of vaccine production from those employed in the 1954 trials had already taken place in 1955, and further changes could be anticipated. Even before the occurrence of poliomyelitis due to inoculation in the spring of 1955, the several states had adopted such surveillance programs. In fact, it was the operation of the program on a state and national scale that led to detection of the first case in Chicago and the outbreaks in California and Idaho. Minnesota began its surveillance program with the first administration of vaccine in the state in May, 1955.

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This paper was presented in preliminary form at the Staff Meeting of the University of Minnesota Hospitals on Feb. 1, 1957.

Changes in production methods were necessitated by at least two phenomena: destruction of antigenicity of type 1 formalinized virus by merthiolate in storage, and the presence of live virus in certain lots of vaccine early in the spring of 1955. The vaccines utilized since October, 1955, cannot be considered as identical with those employed in the field trials of 1954 or in the mass applications late in the spring and in the early summer of 1955. It may logically be argued that removal of merthiolate would operate toward improving the antigenicity of the vaccine; however, there are those who would question the maintenance of antigenicity when additional filtration procedures are applied to guarantee the removal of the last vestiges of live virus aggregates. Although Salk's recent laboratory studies [4] would indicate denial of this possible loss of antigenicity, ultimate proof of maintenance of antigenicity and efficiency of the vaccine would reside in field evaluations.

Finally, the Salk vaccine had had a carefully controlled field trial of adequate magnitude in a nonepidemic year. The question remained whether the vaccine's efficiency would be maintained in epidemic situations and, in fact, afford a rapid decline of poliomyelitis with increasing use.

For these reasons we, in Minnesota, deemed it necessary to conduct a continuous study of vaccine efficacy. In addition to the surveillance program, which would provide constant awareness of vaccine safety, collateral studies were initiated and are continuing on the trend of the incidence of the disease, age distribution of the cases, ratio of paralytic to nonparalytic disease, severity among vaccinated and unvaccinated persons, and the vaccinal status of the population by age. Beginning with the low point of the seasonal cycle of poliomyelitis in April, 1955, every case of poliomyelitis occurring in the state has been investigated intensively for epidemiologic and clinical data and vaccinal status. Although the diagnostic level for paralytic cases was found to be gratifyingly high, all reported cases irrespective of diagnostic category were, wherever possible, subjected to laboratory confirmation. This included attempts at isolation of virus from stools, poliomyelitis antibody titrations on acute and convalescent bloods, and exclusion tests for mumps, St. Louis and western equine encephalitis, and lymphocytic choriomeningitis. These specimens were processed in the laboratories of the Minnesota Department of Health and of the department of bacteriology and immunology of the medical school. Cytopathogenic agents, when isolated in any case, were submitted to the latter laboratory for identification. These latter tests as well as the exclusion tests for the encephalitides assisted greatly in proper designation of nonparalytic poliomyelitis. Physicians of the state as well as hospitals admitting poliomyelitis patients cooperated to an extremely high degree in submitting specimens and providing clinical data to assist in the final diagnosis. This aspect of the study involved personal or telephone communication with attending physicians, visits to major hospitals, and follow-up of patients with regard to residual lesions for severity studies. These studies have yielded interesting information on many aspects of the epidemiology and clinical character of the disease, such as virus types and their geographic distribution, frequency of isolation correlated with age and diagnostic category, contact infection rates, and correlation with symptoms in family contacts, to name but a few. The data reported herein deal exclusively, however, with vaccine efficiency in the two years of its application.

With the success of the field trials in 1954 and the consequent widespread use of vaccine which followed, rigidly controlled studies of vaccine efficacy were no longer possible, though the need for such evaluation obviously remained as indicated above. Methods short of rigid experimental control had to be used, therefore, and several of these have been explored in our evaluation.

Total Poliomyelitis Incidence

If a poliomyelitis vaccine is effective in preventing the disease, it may be argued that its expanding use would naturally affect the total case rate in the population. Consideration of any decline in total incidence must be related to the incidence in an immediately preceding, reasonably long period of time when change in diagnostic criteria or in reporting activity will have been at a minimum. By the end of 1955, approximately 28 million cubic centimeters of vaccine had been distributed in the United States,[5] with 13,500,000 cc. channeled into the National Foundation for Infantile Paralysis (NFIP) program for first and second doses for those participating as controls in the 1954 trials and second doses for those who had received first inoculations in the spring of 1955. Data on actual utilization of vaccine for 1955 are not available for the country as a whole, and the several states had, by the end of the year, developed diverse age priorities. Even if all 28 million cubic centimeters had been used, however, this would have represented but one dose for less than half of the estimated 65 million persons who were in the 0-to-19-year age group or pregnant women. Table 1 shows the reported incidence of poliomyelitis in the nation for the period 1946 through 1956. In 1955, 28,983 cases were reported for a rate of 17.6 per 100,000. In some quarters this was pointed to as a decline due to vaccine and apologies made for the relatively small change on the basis that but a small proportion of the population at risk had been inoculated. Certainly no evidence can be found for a vaccine effect when the 1955 rate was not significantly different from the rate in 1946, 1948, and 1951. By Nov. 30, 1956, an additional 67 million cubic centimeters of vaccine * had been distributed

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and could have represented two doses of vaccine for 30 million and one dose for the remaining 35 million of the 65 million persons at greatest risk for the two-year period. In 1956 there were but 15,400 cases of poliomyelitis reported for a national rate of 9.2. This figure, in line with the trend, could be provocative were it not for the rate of 7.5 per 100,000 in 1947.

TABLE 1.—*Reported Incidence of Poliomyelitis (United States, 1946-1956)*

YR.	No. of Cases*	Rate/100,000
1946	25,698	17.9
1947	10,627	7.5
1948	27,726	18.9
1949	42,033	28.2
1950	33,300	22.1
1951	28,386	18.5
1952	57,879	37.1
1953	35,592	22.4
1954	38,476	23.8
1955	28,963	17.6
1956	15,400†	9.2†

* Source: Annual Supplement, Morbidity and Mortality Weekly Report, National Office of Vital Statistics, Department of Health, Education, and Welfare, Vol. 4, No. 53, Sept. 27, 1956.
† Provisional.

Accurate records of the Minnesota Department of Health reveal that in the spring of 1955, 112,115 children in the first and second grades of school had been given single doses of Salk vaccine under the program of the NFIP, and by the end of the year 181,207 children under 10 years of age (28% of those eligible) had received at least one dose of vaccine while 110,955 (17% of those eligible) of these had received two doses.[7] In addition 6,633 persons between the ages of 10 and 19 and 5,612 pregnant women had received at least one inoculation. In table 2 the reported incidence of poliomyelitis in Minnesota for the period 1946 through 1956, is presented. In 1955, 510 cases were accepted as poliomyelitis for an over-all attack rate of 17.1 per 100,000 which was not significantly different from the rates in 1950 and 1951 and more than twice the rate for 1947. By Dec. 31, 1956, 808,912, or 64.4% of the population aged 0-19 years and pregnant women, who were eligible for vaccination, had received at least one dose with 661,522 receiving two injections.[7] Table 2 reveals the 1956 rate to be 4.5 per 100,000 which, though lowest for the period under consideration, still is not significantly different from the attack rate in 1947. It must also be emphasized that in 1955 and 1956 the total attack rates do not include cases which in earlier years would have been classed as nonparalytic poliomyelitis but which in the study period have been excluded by antibody titrations, encephalitis exclusion tests, and the finding of other cytopathogenic agents. Collateral studies[8] reveal this category to be a significant proportion of the total reported cases. Thus total attack rate data alone at this time are not reliable and may merely portray the marked fluctuation in annual incidence, a well-known characteristic of poliomyelitis.

Incidence of Paralysis

Recalling that the Salk vaccine was statistically shown in 1954 to be effective only against paralytic poliomyelitis, we wondered if a comparison of attack rates for the paralytic disease for the periods under consideration would reveal effect of vaccination. Unfortunately, data on paralytic attack rates for the United States as a whole are not available for earlier than the last few years. Data for Minnesota are available, however, and these are presented in table 2 also. The rate for 1955 was 7.3 per 100,000. This rate would appear promising in comparison to the rates for 1952 through 1954, but it represents twice the rate of paralytic poliomyelitis in 1947 when but 3.7 cases per 100,000 were recorded. In 1956, the first provocative clue is obtained. The rate of 2.1 paralytic cases per 100,000 is almost half the lowest rate recorded in the preceding 10-year period. Although it is essentially true that prior to the delineation of certain poliomyelitis-like diseases and the availability of laboratory tests for their differentiation, a certain number of paralytic cases reported in earlier years were not due to poliovirus, the significant disparity between attack rates for 1956 and 1947 cannot be entirely explained on this basis, for our studies in 1955 revealed that but 6.5% of cases initially reported as paralytic poliomyelitis were ultimately found to have been nonparalytic disease or other entities, such as Guillain-Barré syndrome and transverse myelitis.[8] The extreme variability in paralytic attack rates over the preceding 10-year period in Minnesota, however, makes it difficult to credit the disparity between the rates for 1947 and 1956 solely to the introduction of the vaccination factor in 1956. At least such incidence data cannot reveal what the rate would have been without vaccine.

TABLE 2.—*Reported Incidence and Rates of Poliomyelitis in Minnesota, 1946-1956*

YR.	All Cases		Paralytic Cases	
	No.	Rate/100,000	No.	Rate/100,000
1946	2,881	96.6	1,824	61.2
1947	201	6.7	110	3.7
1948	1,387	46.5	683	22.9
1949	1,715	57.5	880	29.5
1950	502	16.8	266	8.8
1951	511	17.1	262	8.8
1952	3,926	131.6	2,041	68.4
1953	2,137	71.7	1,137	38.1
1954	649	21.5	309	10.4
1955	510	17.1	218	7.3
1956	145*	4.5	67	2.1

* Provisional with respect to nonparalytic cases only.

Ratio of Paralytic to Nonparalytic Disease

Assuming that the ratio of paralytic cases to nonparalytic cases would be reversed in favor of nonparalytic cases as a vaccine effect, an evaluation

of vaccine efficiency might be made on the basis of proportion of paralytic cases. Table 3 presents the annual proportions of paralytic cases for Minnesota in the period 1946-1956 and for the entire nation in the period 1951-1956. The values for the United States as a whole are not reliable since large proportions of the reported cases were undesignated as to type of disease. The data for Minnesota, however, are complete. In the period prior to 1947 the proportion of paralytic cases was much higher than in the past 10 years. An increasing trend in reporting of nonparalytic cases was noted then, and this trend became stabilized from 1947 onward. Thus it can be noted that in the vaccine years 1955-1956 the proportions of paralytic cases were somewhat lower than the rather stable proportions in the preceding eight-year period but not as low as might be expected from the increasing use of Salk vaccine

TABLE 3.—*Percentage of Reported Cases Designated as Paralytic by Year of Report (Minnesota 1946-1956; United States 1951-1956)*

Yr.	Minnesota	U.S.*
1946	63.3	...
1947	55.2	...
1948	51.4	...
1949	51.2	...
1950	58.3	...
1951	51.5	**64.7**
1952	52.0	**62.4**
1953	53.1	**56.3**
1954	48.4	**58.1**
1955	42.7	**52.7**
1956	46.2	**53.4**

* Sources: Annual Supplements, Morbidity and Mortality Weekly Reports, National Office of Vital Statistics, Department Health, Education, and Welfare, 1953-1956.

in this two-year period. It should be noted, however, that the only comparable years in the series are 1955 and 1956. From the inception of the surveillance program in 1955, classification of cases has involved more rigid criteria than in the preceding eight-year period. It is obvious, then, that if poliomyelitis-like disease without paralysis had been included in 1955 and 1956 the proportions of paralytic cases would have been still smaller. By including the nonparalytic poliomyelitis cases of 1955 and 1956 as originally reported to the department of health without rigid clinical review and resort to laboratory data, the proportions of paralytic cases in the total reported incidence for the years 1955 and 1956 would have been 38.0% and 30.7% respectively. These values, which thus become more nearly comparable to the values for the preceding period, do represent significant reductions in the proportions of paralytic attacks and correlate well with the increasing application of Salk vaccine to the Minnesota population. Although providing a clue to vaccine efficacy, this indirect approach is at best only inferential.

Age-Distribution Studies

In 1955 vaccine had been given primarily to Minnesota children within the age group 5-9 years. (Only late in October were inoculations begun in children under 5 and in December in persons in the age group 10-19 [table 4].) Evidence for vaccine efficiency might be sought in an age shift in paralytic attack rates away from the 5-to-9-year group, especially since this group had yielded higher paralytic attack rates than all other age groups in the preceding nine years with the exception of 1951. In figure 1, age-specific attack rates for paralytic poliomyelitis in Minnesota have been plotted as average rates for the period 1951-1953 and as individual rates for 1954, 1955, and 1956. The curve for 1955, though showing a moderate tendency to flatten, nevertheless revealed a continuing peak at age 5-9. This, of course, would be expected in view of the fact that in Minnesota in 1955 only 112,115

TABLE 4.—*Reported Inoculations with Salk Vaccine Among Persons 0-19 Years of Age and Pregnant Women (Minnesota 1955-1956)*

Period	Age Group, Yr.	Inoculation			Total Inoculations
		First	Second	Third	
5/55- 6/55	1st and 2nd grades	112,115	...	...	112,115
9/55-10/55	1st and 2nd grades	...	106,753	...	106,753
10/17/55-12/31/55	Under 5	42,870	2,571	7	45,448
	5-9	96,222	1,631	3	97,856
	10-14	5,118	140	...	5,258
	15-19	1,515	23	...	1,538
	Pregnant women	5,612	449	1	6,062
1/1/56-12/31/56	Under 5	237,323	234,069	22,228	474,220
	5-9	137,383	138,502	27,532	303,418
	10-14	129,873	111,194	10,307	251,374
	15-19	59,255	46,370	3,289	108,914
	Pregnant women	51,626	39,219	218	91,063
Total 1955-1956		888,912	661,522	63,585	1,534,019

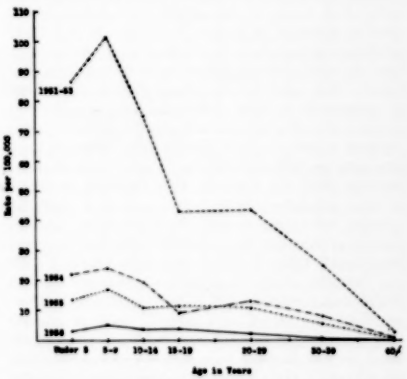

Fig. 1.—Age-specific attack rates of paralytic poliomyelitis in Minnesota, 1951-1956.

children, predominantly 6 and 7 years of age, out of 287,158 in the 5-to-9-year age group had received but a single dose of vaccine in May and June. In consolidated age distribution data from 33 states in 1955, there was noted an unprecedented and significant lowering of the paralytic attack rates among children 7 and 8 years old. This discontinuity was even more striking when the curve was superimposed on that for 1952.[9] These ages represent the bulk of children vaccinated in the field trials of 1954, with boosters in 1955, as well as those in the NFIP programs of 1955. A similar finding on hospital admission data was reported by the NFIP.[10]

For 1956, the tendency to flattening of the age-specific paralytic attack rate curve for Minnesota is greatly exaggerated. The minor differences in age-specific attack rates among the groups under 20 years of age are very insignificant. This would be expected if due to a vaccine effect, since more than 95% of the 5-to-9-year age group in the state have had at least one dose of vaccine and more than 77% have had two doses (table 5).

Two other states, New York and California, have compiled and released data similar to those of Minnesota. The New York data are graphically portrayed in figure 2. Not only has the curve of age-specific paralytic attack rate been flattened, but the rates for the age groups 5-9 and 10-14 are significantly lower than for the group under 5 years. California, with an increase in cases over that of 1955, a trend distinctly different from that of New York and Minnesota, noted a shift in age incidence from the 5-to-14-year group to the group under 5 years of age. These data for the three states seem to correlate well with the proportions inoculated in the several age groups. Also, data for the nation at large (which data are as yet incomplete) would indicate a distinct trough in the age-specific paralytic attack rate curve between the 5-year and 9-year age groups.[11]

This type of evidence is highly suggestive of a vaccine effect, and we would be prone to accept it unequivocally as indicative of vaccine activity were it not for the epidemiologic history of poliomyelitis. Our reluctance to do so, minor though it may be, is based on the fact that early in the history of the disease the greatest risk of attack occurred among children under the age of 5. Since we do not understand all the natural factors which produced a shift in attack to older age groups, it would be folly to assume these factors could not provide for a reversal of age-incidence trends. Slight though this possibility may be, the significance of these shifts must await long-term analyses and, wherever possible, comparisons between communities with high and low levels of immunization in the same period of time.

TABLE 5.—*Estimated Vaccination Coverage of Selected Age Groups (Minnesota, Dec. 31, 1956)*

Age Group, Yr.	% with 1 Dose	% with 2 Doses	% with 3 Doses	% with Any Vaccine
0-4	17.0	52.7	6.0	75.7
5-9	10.0	76.4	9.6	96.0
10-14	9.3	39.6	4.0	52.9
15-19	6.4	18.0	1.5	25.9
0-19	11.4	49.2	5.6	66.2

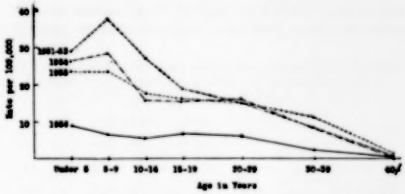

Fig. 2.—Age-specific attack rates of paralytic poliomyelitis in New York State, 1951-1956 (source: C. D. Bulletin, N. Y. State Health Dept., Dec. 28, 1956).

Rates Among Vaccinated and Unvaccinated

The most nearly adequate proof of vaccine efficacy must, therefore, reside in the comparison of attack rates for vaccinated and unvaccinated groups of similar ages and under similar circumstances of exposure. The conditions for such continued field testing presented themselves in Minnesota in 1955 when vaccine, in short supply, was restricted to first and second-grade school children. In Minnesota, which did not participate in the 1954 trials, a virgin population was available for a study of effectiveness of a single dose of vaccine. In the last week of May and first week of June, 1955, 112,115 of 145,374 eligible school children received a single dose of Salk vaccine. The evaluation period was selected to begin on June 1, since the vast majority of eligible school children had by then had the first dose of vaccine. The closing date was Oct. 1. By this time the peak incidence of the disease had passed and second doses had just been given. In this period there occurred 20 cases among the inoculated and 9 cases among the uninoculated first and second graders. An additional or check control of unvaccinated 6-to-9-year-olds was also utilized, since it was felt that cases occurring among unvaccinated first or second grade children older than 8 years might not be brought to our attention as part of the study group for this latter group was grade-designated rather than age-designated. Since an independent survey showed that the proportions of 5-year-olds in the first grade and 10-year-olds in the second grade in May, 1955, were negligible, the auxiliary control group was limited to 6-to-9-year-olds. In this latter group 37 cases occurred. Table 6 presents the case rates of the study and control groups for the period June 1 to Oct. 1 according to

type of disease. Pertinent to our discussion are the paralytic attack rates which revealed a definite protective effect by a single dose of vaccine. The virtually identical rates for the two types of control are of interest.

Although the figures for Minnesota are small and the group differences not of high statistical significance, the collective experiences of special studies in other states in 1955, especially those with epidemics, support these findings.[12] No evidence to the contrary was educed in 1955. States with adequate data for single dose evaluations included California, Massachusetts, New York (upstate), and Wisconsin. California, with a paralytic attack rate among nonvaccinates comparable to the Minnesota experience, showed a 59% reduction among vaccinates. New York State (exclusive of New York City) with a slightly higher paralytic rate revealed a 76% reduction. Massachusetts and Wisconsin both experienced type 1 epidemics in 1955. A paralytic rate of 157 per 100,000 among unvaccinated persons in Massachusetts[13] may be compared with a rate of 63 among vaccinates for a reduction of 60%. Wisconsin, with the second highest case rate in the nation,[12] showed a 72% reduction (from 102 to 29 per 100,000) among vaccinates. These and other states revealed greater percentages of effectiveness with two doses of vaccine: California, 88%; Canada (selected provinces), 100%; Louisiana, 89%; Massachusetts, 65%; New York, 86%; North Carolina, 60%; and Wisconsin, 84%. Thus, in 1955, the collective experience with one and two doses of vaccine yielded consistent evidence of continued efficacy of the vaccine.

As discussed earlier, since changes in procedure of vaccine production were continuing, we in Minnesota deemed it necessary to establish continuous evaluation of vaccine efficiency. As vaccine supplies were increased after September, 1955, broader age groups were encompassed and by early 1956 the group 0-19 years of age and pregnant women of any age were included among the eligible priorities. The situation after Oct. 17, 1955, was quite different from that which prevailed in the spring of 1955 when a single dose was given to a large group in a short period of time. Vaccinations were being performed throughout the year, before, during, and after the seasonal peak of the disease. Some individuals were receiving their second and even third doses while others were receiving their first. Thus the several age groups as well as individuals within an age group were subjected to varying risk of attack, first as nonvaccinates and then as recipients of one, two, or three doses of vaccine. It is apparent that the vaccination status of the population was, and continues to be, a continuously varying quantity. It is immediately obvious that the simple analysis applied to the 1955 data was no longer valid under such circumstances. A "pure" group, with constant vaccinal status to be carried through a poliomyelitis season intact, no longer existed.

To compensate for this, a "life-table" approach was utilized in computing case rates. The denominators were no longer stable segments of the population but rather person-months or person-years of experience in categories of unvaccinated, one-dose, and two-dose rank. A case of poliomyelitis occurring in any of the categories was considered as leaving that category. Similarly those receiving a second dose of vaccine were considered as leaving the one-dose category and those receiving a first dose as leaving the unvaccinated category. To compute the number of person-months at risk in a certain category, to the number present in the category at the beginning of the month add one-half the number entering the category during the month and subtract one-half the number leaving the category during the month. Halving the latter two numbers is done to compensate for the fact that individuals do not leave or enter en masse on the first day of the month but do so continuously throughout the month. To obtain the person-years value, divide the total number of person-months by 12. To obtain the vaccinal status of members of the

Table 6.—*Poliomyelitis Case Rates per 100,000 Among Children in First and Second Grades (Minnesota, 1955; Onsets June 1-Oct. 1)*

Group	No. of Children	Total Cases	Total Rate	Nonparalytic Cases	Nonparalytic Rate	Paralytic Cases	Paralytic Rate
Vaccinated (1 dose) 1st and 2nd grades	112,115	20	17.8	16	14.3	4	3.6
Control: nonvaccinated 1st and 2nd grades	33,259	9	27.0	5	15.0	3	9.0
Control: nonvaccinated 6-to-9-year-olds	141,023	37	26.2	25	17.7	12	8.5
Protection afforded	...	...	34%	...	(5%)	...	60%

Table 7.—*Person-Months of Experience by Immunization Status (Minnesota, June 1, 1955-Dec. 31, 1956)**

Month	No Vaccine	1 Dose	2 Doses	Age Groups Considered, Yr.
June, 1955	33.3	112.1	...	1st and 2nd grades
July	33.3	112.1	...	1st and 2nd grades
August	33.3	112.1	...	1st and 2nd grades
September	33.3	112.1	53.4	1st and 2nd grades
October	140.7	5.7	106.8	6-9
November	109.5	10.9	106.8	5-9
December	498.4	50.0	198.9	0-9
January, 1956	888.4	119.3	125.6	0-19
February	796.1	184.2	152.2	0-19
March	743.9	212.3	177.2	0-19
April	680.0	237.6	205.7	0-19
May	609.4	286.3	237.7	0-19
June	534.5	291.7	307.2	0-19
July	487.2	241.3	465.9	0-19
August	454.2	197.8	481.4	0-19
September	428.4	170.1	534.8	0-19
October	411.6	151.9	569.8	0-19
November	399.4	138.0	595.9	0-19
December	386.1	127.1	619.6	0-19
Total person-mo.	7,637.9	2,424.2	4,735.6	
Person-yr.	636.5	202.0	394.6	

* All figures in thousands.

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population month by month, continuous tabulations of all vaccine inoculation reports from physicians and clinics were maintained. These reports were on a mandatory basis for the duration of the distribution of state-purchased vaccine and on a voluntary reporting basis for commercial supplies after these were available in August, 1956. In Minnesota, 100% of available vaccine was state-purchased through July, 1956. Although no restrictions on age use were placed on commercially purchased vaccine, only the 0-to-19-year group was studied for vaccine efficiency. Furthermore, vaccinal status was arbitrarily deemed to change 14 days after date of inoculation to provide for adequate vaccinal effect. Thus, if the date of onset of a case was within 14 days of the date of last dose of vaccine, that dose was discounted. (It is recognized that any dose of vaccine administered to an individual with preexisting naturally acquired antibody may well evoke a booster response in much less time than this. Since the existence of such antibody was not known in any of the cases, the 14-day interval was selected for the sake of uniformity.)

In table 7 are the data on person-months of experience or risk, by immunization status. It will be noted that the first and second grade groups have been included in our most recent calculation since they not only are obviously part of the 0-19 group, but have had second doses of vaccine since the summer of 1955 and have had two seasons of exposure to poliomyelitis. The total person-months and person-years for each category from which attack rates have been calculated are also noted. In table 8 is the distribution of cases of poliomyelitis occurring in the study period according to clinical types, vaccinal status, and period of occurrence. Utilizing these data as numerators and the date

TABLE 8.—*Cases of Poliomyelitis with Onset Between June 1, 1955, and Dec. 31, 1956, by Vaccination Status, Clinical Types, and in Selected Age Groups (Minnesota)*

Time Period	Age Group, Yr.	Paralytic			Nonparalytic		
		No Vaccine	1 Dose	2 Doses	No Vaccine	1 Dose	2 Doses
6/1/55-9/30/55	1st and 2nd grades	3	4	...	5	16	...
10/1/55-10/31/55	0-9	3	...	...	1	...	2
11/1/55-11/30/55	0-9	4	...	...	...	...	...
12/1/55-12/31/55	0-9	1	...	...	...	...	...
1/1/56-12/31/56	0-19	38	8	5	27	5	15
Totals		49	12	5	33	21	17

from table 7 as denominators, attack rates by vaccinal and clinical status are derived and expressed in cases per 100,000 person-years of experience. These are summarized in table 9. It can be seen that reductions in incidence of paralysis occurred both in the population with single doses of vaccine and in that with two doses of vaccine. Reduction in rate or protection afforded by one dose was 23.4%, a difference found not to be significant. With two doses however, the reduction was 83.1%, a highly significant difference.

Possibilities of Error and Questions Remaining.—It was anticipated that questions on the validity of use of commercial vaccine data would arise because of incompleteness of voluntary reporting. To test the magnitude of the error involved, copies of com-

TABLE 9.—*Poliomyelitis Attack Rates, per 100,000 Person-Years of Experience, by Clinical Type and Vaccination Status (Minnesota, June 1, 1955-Dec. 31, 1956)*

Vaccinal Status	Total Cases	Total Rate	Nonparalytic Cases		Paralytic Cases	
			No.	Rate 100,000	No.	Rate 100,000
No vaccine	82	12.9	33	5.2	49	7.7
1 dose	33	16.3	21	10.4	12	5.9
2 doses	22	5.6	17	4.3	5	1.3

mercial vaccine shipment invoices, inventories of unused vaccine in the hands of physicians, pharmacists, and distributors, and voluntary reporting data on the use of commercial vaccine were analyzed. From these sources it was calculated that voluntary reporting for the months of August through December, 1956, was approximately 59% complete. However, theoretically adjusted values of commercial vaccine application in the 0-to-19-year age group represented a maximum of 1.1% of all the vaccine used for the first dose in the total experience and 2.2% of all the vaccine used for second doses in this experience. Thus, errors in the denominators, interjected by incompleteness of voluntary reporting, cannot exceed these magnitudes. In any event, perfect reporting would obviously have increased the denominators for the single and two-dose categories and diminished the unvaccinated denominator. Hence disparities in paralytic attack rates between the vaccinated and unvaccinated groups would have been increased in favor of the vaccinated.

Thus it may be concluded that Salk vaccine as utilized in Minnesota maintained relatively high protective efficiency when two doses were given. The percentage reduction in paralytic attack with a single dose of vaccine for the experience as a whole, though statistically not significant, was smaller than the protection afforded by a single dose in the 1955 season. Whether this implies a moderate decline in antigenicity in present vaccines over those utilized early in 1955 cannot be stated with assurance from these data. It is significant, however, that two doses provided a degree of protection comparable to that provided by three doses in the field trials of 1954. This is not surprising in view of Salk's subsequent investigations [14] in which it was shown that the third inoculation in the 1954 field trials, one month after the second inoculation which had been given a week after the first, was, indeed, not a booster dose; and antibody levels following this third injection were not significantly

higher than the levels following the second inoculation. In 1955 and 1956, recommended immunization schedules in Minnesota and elsewhere followed Salk's recommendation of a month's interval between first and second inoculations and no less than seven months between second and third inoculations.

The practical application of vaccine efficiency to epidemic theory is pertinent since the occurrence of outbreaks in the face of intensive immunization programs in some areas could prompt premature judgment of vaccine failure. Doubt of vaccine efficacy could be expressed in considering the outbreak of poliomyelitis in Chicago early in the season in 1956. When incidence began to rise early in July, sufficient vaccine had already been used to provide for two inoculations in slightly less than 50% of the eligible population under 20 years of age, the group at greatest risk. In an upstate New York county with a population of 100,000, the attack rate by September, 1956, had reached 100 per 100,000. It was estimated that close to 50% of the eligible population had been vaccinated.

Do these instances of increased poliomyelitis incidence signify vaccine failure? It will be recalled that in Massachusetts during the large outbreak of 1955 a single dose of vaccine was proved to effect a 60% reduction in paralytic attack rates[13] from 157 per 100,000 among unvaccinated to 63 per 100,000 among the vaccinated. In Wisconsin, under epidemic conditions a similar reduction in rate was achieved. The rates for vaccinated were nevertheless higher than those for unvaccinated populations in nonepidemic states. Where, then does the explanation of this seeming discrepancy lie?

Poliomyelitis vaccination apparently does not prevent infection with the virus. In animal studies extremely high titers of antibody are necessary to reduce multiplication of virus.[15] In man virus continues to multiply and to be excreted from the stool after vaccination and antibody rise, although there is some evidence that the period of excretion may be shortened. The dynamics of poliomyelitis epidemics are not entirely understood. Favorable balance between susceptibles and immunes in the population provides an oversimplified explanation for a phenomenon which must involve, among other factors, the quantity of virus in a community and its rapidity of spread. The history of poliomyelitis in any community reveals swings of incidence, both in total and in paralytic categories, from extreme lows to extreme highs. The number of paralytic cases that will occur in a community is unpredictable. In 1955, the attack rates in many communities were low; in Minnesota this was also true. Since only 10% of the population at greatest risk (0-19 years of age) had received but a single dose of vaccine, certainly the low paralytic rate cannot be entirely attributed to vaccine. In Massachusetts a corresponding percentage of the same-aged population had received vaccine but the over-all rate was much higher. A difference in effective spread of virus must have occurred. With so small a fraction of the population at risk vaccinated with an antigen providing but 60-70% protection against only the paralytic form of the disease and not preventing infection per se, the ubiquitous virus obviously came into contact with large numbers of susceptible unvaccinated individuals. To these must be added the vaccine failures, for, at best, a 60-70% or even 80% effective vaccine allows the development of paralytic cases in an amount equal to 20-40% of the paralytic cases which would have occurred had vaccine not been given in the community.

At what level of vaccination could we be sure that outbreaks would no longer occur? The answer to this is not available at the present time nor is it simple to derive on theoretical grounds. In Minnesota, only 49% of the population 0-19 years of age had received two doses of vaccine by the end of 1956 (table 5), and 34% of this population group remained without a single dose. The Chicago and upstate New York experiences would indicate that immunization of 40-50% of the population at greatest risk is not adequate. The low paralytic attack rate in Minnesota in 1956 must in part have been due to vaccine; but the greatest part of this rate and virtually all of the rate in 1955, also quite low, may have been but manifestations of a more or less cyclic phase in the dynamic balance between natural immunity and susceptibility.

Will vaccination virtually approaching 100% in a community ultimately lead to a reduction in carrier infections or at least in their duration and thus reduce the opportunities for transfer of virus? Will communities, achieving such a state of affairs, and maintaining antibody levels on a continuing basis, by early infancy immunization and boosters, ultimately rid themselves of epidemic threats and bypass the phenomenon of vaccine failures so that paralytic cases will occur but rarely? These are among the problems that the ensuing years of observation may resolve. At the present time, and pending the development of even more efficient poliovirus vaccines, vaccine coverage of an even larger proportion of the population is an immediate goal.

Summary

The use of trends in total and paralytic attack rates as measures of poliomyelitis vaccine efficiency has been found inadequate. Paralytic attack ratios and age-distribution comparisons have been found only suggestive of vaccine efficacy. The most nearly adequate measure of vaccine efficiency, short of placebo control studies, appears to be comparison of paralytic attack rates between comparable vaccinated and unvaccinated groups.

To permit the comparison of paralytic attack rates among vaccinated and unvaccinated groups constantly varying in a population, a "life-table" method has been developed. By this method, analysis has revealed the use of two doses of Salk poliomyelitis vaccine in Minnesota in 1955-1956 to have been 83% protective against paralytic poliomyelitis. The continuing evaluation of vaccine efficiency will depend on cooperation of all physicians in the voluntary vaccination reporting system.

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CLINICAL NOTES

PARAPLEGIA AFTER TRANSLUMBAR AORTOGRAPHY

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Translumbar aortography has become a widely employed procedure. It has been considered relatively safe and it is not difficult to perform. Although there have been only a few recorded cases of paraplegia secondary to abdominal aortography, this is a complication of great magnitude. A review of the literature reveals five cases reported by Antoni and Lindgreen (1949),[1] Boyarsky (1954),[2] Baurys (1954),[3] Abeshouse and Tiongson (1956),[4] and McCormack (1956).[5] There are undoubtedly other instances of paraplegia after this procedure which have not been reported. Baurys states that Nelson was acquainted with two cases which occurred in Europe and Canada respectively. Another unreported instance is referred to in an insurance journal.[6] The following report places on record still another instance of this catastrophic complication of aortography.

From the departments of medicine and surgery, Vanderbilt University School of Medicine.

Report of a Case

A 50-year-old man was first admitted to Vanderbilt Hospital in June, 1949, because of hypertension, hypertensive headache, and retinal hemorrhages. The blood pressure was 180/100 mm. Hg. One month later he was readmitted and a bilateral thoracolumbar sympathectomy was performed. Subsequently, hypertension persisted and the patient experienced short periods of mental confusion interpreted as being due to hypertensive encephalopathy. From 1949 to 1956 he was frequently admitted to a local hospital for treatment of hypertension. In 1954 a chronically infected and contracted left kidney was removed surgically.

On Sept. 20, 1956, he was admitted to Vanderbilt University Hospital because of pain and numbness in the right leg and foot, both at rest and upon exercise, of six weeks' duration. Walking was accompanied by a limp. The pain became so severe for three weeks before admission that frequent injections of opiates were necessary. Some pain, less severe, occurred in the left leg and left foot.

Examination revealed a thin, emaciated man who appeared 10 years older than the stated age. Retinal and generalized arteriosclerosis were present. The heart was enlarged. The blood pressures in the recumbent, sitting, and standing positions were, respectively, 160/85, 120/78, and 90/68 mm.

Hg. The lower third of the right foot was the site of rubor on dependency and was cool. Both femoral arteries were felt but the pulsations were slightly diminished and no pulsations whatsoever were detected in the more distal vessels. Limping and dragging of the right foot characterized the gait.

The maximum urinary concentration was 1.008. The blood nonprotein nitrogen level was 44 mg. per 100 cc., and the serum cholesterol level was 270 mg. per 100 cc. X-ray of the lower extremities did not show any arterial calcification. An electrocardiogram revealed the changes of left ventricular strain and anterior wall coronary insufficiency.

It seemed likely that there was present either a partial thrombotic occlusion of the terminal abdominal aorta or of the right femoral artery. On Sept. 27, 1956, an aortogram was made. With the patient under light anesthesia with thiopental (Pentothal), two needles were inserted via the lumbar region into the abdominal aorta. A test dose of 1 ml. of a 70% solution of acetrizoate (Urokon) sodium was injected. No evidence of sensitivity developed. Injection of acetrizoate through each needle was then begun. The cassette changer on the x-ray table became jammed on the third film, and because of this fact the injection was discontinued after a total of 12 ml. Slight extra-aortic extravasation occurred. The two films showed an incomplete picture of the aorta. There was retrograde filling and the 12th left intercostal artery was visualized. It was decided to repeat the injection. This was done 15 minutes after the first injection. The needles were reinserted at a lower level and 10 ml. from each syringe was injected simultaneously. The aortograms revealed conclusive evidence of blockage of the aorta below the level of the body of the third lumbar vertebra. The column of dye extended upward instead of downward and the lower part of the aorta could not be visualized. The procedure was completed at 3 p. m. At 5 p. m. a flaccid paralysis of the lower extremities became evident and there was anesthesia below the 11th thoracic dermatome. Vibratory and position senses were absent, as were the deep reflexes in the lower extremities. A neurologist confirmed the presence of transverse myelopathy at the 11th thoracic segment.

After four months the neurological manifestations of the transverse lesion persisted without any change. The intractable pain in the foot and leg disappeared with the onset of anesthesia. Catheter drainage has been complicated by several exacerbations of urinary tract infection. Physiotherapeutic measures have been employed. Recently, an infarct developed in the lower lobe of the left lung, and the patient's condition remains precarious.

Comment

The exact cause of paraplegia in our patient is not known. In four similar cases reported, paraplegia was a complication of indirect abdominal aortography, and McCormack [5] reports its development after a direct aortogram carried out at the time of left lumbar sympathectomy. At autopsy thrombosis of the anterior spinal artery and its branches has not been demonstrated. Demyelinization has been observed in the thoracolumbar region of the cord, with principal involvement of the lateral funiculi and of the ventral funiculus. Boyarsky [2] theorized that sensitivity of the nervous system to the contrast medium was present in the case he observed. Hol and Skjerven [3] emphasized that damage to the spinal cord after translumbar aortography may be expected from the supine position of the subject, prolonged exposure to the contrast medium, repeated injections of the contrast medium at short intervals, and abnormal susceptibility of the spinal cord to injury. They suggest that the high specific gravity of the contrast medium predisposes to concentration of the material in the dorsal arteries supplying the spinal cord. They note the possible causative role of prolonged exposure to the contrast medium resulting from retardation of the blood flow in cases of thrombus formation. Abeshouse and Tiongson [4] also believe that paraplegia results from spinal cord damage produced by the direct toxic action of the highly concentrated contrast medium and they discuss the possible etiological role of vasospasm.

In their cases, Antoni and Lindgreen [1] employed a 70% solution of iodopyracet. Boyarsky's patient [2] developed paraplegia immediately after aortography with a 70% solution of acetrizoate. The type of contrast medium employed by Baurys [6] is not known. Abeshouse and Tiongson [4] used a 70% solution of acetrizoate. McCormack [5] also employed this drug in the same concentration, and so did we.

In our case and in two of the other five which have been reported (Boyarsky [2] and McCormack [5]), the initial aortograms were considered unsatisfactory and were promptly repeated. Because transverse myelopathy developed after the reinjections, McCormack suggests a delay of from 7 to 10 days when a second aortogram is required. He also suggests a higher injection level since this provides an increased number of collateral channels for the distribution of the dye and increases the opportunity for dilution. Since sensitivity of the spinal cord to various contrast chemicals may vary directly in proportion to their concentration, a 50% solution instead of a 70% solution of diatrizoate (Hypaque) sodium has been employed by some workers.

The injection level in our case was possibly a little higher than usual, since the dye extended upward and the lower intercostal arteries were visualized. It was felt that the lumbar sympathectomy and the left nephrectomy which the patient had undergone previously distorted the position of the aorta to some extent.

Other complications of translumbar aortography occur. Gould and Willson,* in a review of the various complications of aortography, describe six cases in which severe renal damage followed the injection of renal arteries. They cite eight instances of renal shutdown, two of which were fatal, after injections of the dye into the aorta. Thrombosis of the superior mesenteric arteries has also been observed.

Our unfortunate experience with aortography, reviewed in the light of the experience of others, has led us to abandon it as a diagnostic procedure. If the clinical story suggests occlusive disease of the lower abdominal aorta or if an aneurysm thereof has been detected, then, by direct surgical approach the femoral arteries are visualized. This takes only a few minutes. If the femoral vessels are patent and relatively free of arteriosclerotic change, the

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primary operative procedure, be it replacement grafting or thromboendarterectomy of the occluded portion of the aorta, is then carried out. When, because of the history and physical signs, a block of the femoral artery is suspected, the popliteal vessels are initially exposed and examined. Although formerly direct aortography or arteriography was employed on occasions during surgery, we have also abandoned this practice.

Summary

Transverse myelopathy with paraplegia is a complication of translumbar aortography. The indications for this diagnostic procedure, employing the opaque mediums currently available, are rarely sufficient to justify the risk involved. Surgical exposure and direct examination of the aorta and its branches is the optimum method of examination at this time.

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EARLY CLUE TO VISCERAL CARCINOMA—HEMORRHAGE AFTER INTRAVENOUSLY GIVEN WARFARIN

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A clue to the possible presence of an obscure visceral carcinoma, notably, carcinoma of the pancreas, may arise from the hemorrhage which appears within 24 hours after the intravenous administration of the highly potent and prompt-acting anticoagulant, warfarin (Coumadin) sodium.[1]

The case presented below, coupled with a previous experience with thrombosis, may show this procedure to be an important diagnostic tool. The appearance of early bleeding in this patient, markedly contrasting that noted in previous experience with over 125 intravenous injections of warfarin, leads me to report this case in the hope that others with more clinical material available may be led to assess the usefulness and limitations of the suggested test. Fortunately, the availability of phytonadione (vitamin K_1, Mephyton) reduces the hazards associated with the hemorrhage. Vitamin K_1 promptly counteracts the bleeding produced by warfarin.

A consideration of the recent literature associating thrombosis and carcinoma lends credibility to the proposed test. Several observers [2] have stressed that early recognition of thrombophlebitis is a possible clue to cryptic or obscure malignant lesions. Wright [3] noted that thrombophlebitis associated with malignancy resists anticoagulant therapy with bishydroxycoumarin (Dicumarol), even though the prothrombin activity is depressed to therapeutic levels.

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Report of a Case

A 60-year-old female weighing 168 lb. (76.2 kg.) entered the hospital on Oct. 15, 1955, complaining of severe pain and swelling along the entire left arm. Four months prior to admission, she noticed for the first time a pain and a swelling of the left foot, which spread to the right foot, leg, and thigh. Treatment at home with bed rest and elevation of the feet resulted in subsidence of the pain and swelling. There had been no chills or elevation of temperature. She was not aware of any apparent injury to the arms or legs; she had not undergone surgery or been bedridden; there was no weight loss. Her personal and family histories were normal.

On admission, a diagnosis of thrombosis of the left axillary vein was made. One 50-mg. dose of warfarin was administered intravenously. Prior to administration of the anticoagulant, her prothrombin time was 24 seconds, or 33% of normal (control 15 seconds). Questioning revealed that the patient had not previously received any anticoagulants or other medicaments. Twelve hours after the injection, bleeding at the venipuncture site and gross hema-

turia appeared. The prothrombin activity was infinity (prothrombin activity 0% after two hours). The oozing of blood from the puncture site was controlled by a pressure dressing. Twelve hours after the injection of warfarin, 75 mg. of phytonadione was administered intravenously. The bleeding from the puncture site and the hematuria cleared within eight hours. On the following morning, the prothrombin time was 33 seconds (20% of normal, control 15 seconds). Hematological studies revealed no evidence of any blood dyscrasia. Six days after admission, the swelling and pain subsided and she was discharged from the hospital. The presence of a malignancy was not entertained.

Three weeks after discharge, she returned to the hospital with complaints of severe headache and an inability to talk. A motor aphasia prevented communication. It was felt that the patient had a cerebral thrombosis. Recalling the profuse hematuria after the administration of the anticoagulant on the first hospitalization and the previous thrombotic episodes, we now suspected the presence of a malignancy, particularly of the body of the pancreas. Venous and arterial thrombosis became more prominent. The patient's condition was progressively worsening, with gangrene of the right great toe (demarcation at the metatarsophalangeal joint) and hemiplegia. Permission for a laparotomy could not be obtained. She died on the 32nd hospital day.

In summary, then, this patient exhibited multiple thrombosis characterized in succession by (1) bilateral thrombophlebitis of the lower extremities, (2) axillary vein thrombosis of the left arm, and (3) cerebral thrombosis and finally arterial thrombosis exhibited by gangrene of the great toe. The antemortem diagnosis of carcinoma of the body of the pancreas was confirmed by autopsy.

Postmortem Findings.—Postmortem examination of the pancreas revealed an infiltrating adenocarcinoma of the body of the pancreas with metastatic adenocarcinoma to the regional lymph nodes, liver, and lungs. There were multiple venous thrombi, involving the veins of the lower extremities and the pelvis. In the heart, mural thrombi were noted on the tricuspid and mitral valve leaflets. The pulmonary arteries contained multiple small emboli of varied ages.

Microscopic examination of sections of the pancreas showed it to be infiltrated by a gland-forming tumor. There were severe disparities of nuclear size, shape, and staining effect. The cytoplasm of the tumor cells was granular or vacuolated, and the tumor had a desmoplastic reaction. Occasionally preserved islets were seen within tumor masses. The tumor was seen in perineural lymphatics. Some of the sections of the pancreas showed an essentially normal architectural pattern with no duct dilatation.

Sections taken from many pelvic and leg veins showed striking examples of occlusive thrombosis with recanalization and deposition of iron pigment.

The branches of the pulmonary arteries of all sizes showed many old and recent, occasionally recanalizing, thrombi. At the periphery of the lungs were small focal collections of tumor, the details of which were similar to those in the pancreas.

Organizing fibrin masses appeared on the endocardial surfaces of the heart. The right ventricle had a normal epicardium and myocardium, but the endocardium was abnormal in that organizing masses of fibrin were present on the tricuspid valve leaflets. No bacteria were seen. There were no inflammatory changes in the valves.

Sections of the adrenals, ovaries, cervix, gastrointestinal tract, and spleen were unremarkable. Sections of the brain and upper cervical cord were essentially normal.

Comment

The association of thrombophlebitis and visceral cancer is well known. Although Trousseau first noted this association in 1856 [4] and Osler did in 1900, Sproul's study [5] in 1938 reawakened an interest in this matter. Since then, other reports reemphasized the association between thrombosis and carcinoma.[6] Following are possible early clues to cryptic malignant lesions [6]: (1) an unexplained episode of pulmonary embolism,[2f] (2) at least two bona fide episodes of thrombophlebitis, regardless of the location, mildness, or shortness, provided the thrombophlebitis cannot be satisfactorily explained on some other basis (even a single bout of apparently spontaneous thrombophlebitis should arouse suspicion if there are other new systemic symptoms or a recent change in previous symptoms [2f]), (3) refractoriness of an episode of thrombophlebitis to adequate anticoagulant therapy or unexplained bleeding with prothrombin times in the therapeutic (up to 40 seconds) range,[3] and (4) the initiation of bleeding, sometimes profuse, of a gastrointestinal carcinoma when the patient is receiving anticoagulant therapy.[2g]

To those observations now may be added the hyperreaction to the established prompt action of warfarin. A single dose of this drug may result in prothrombin depletion and in hemorrhage in contrast to the usual high tolerance to 1 mg. per kilogram of body weight of warfarin. The hyperreaction may manifest itself by gross hematuria and continuous oozing from the venipuncture sites. In the absence of any evidence of a blood dyscrasia after appropriate hematological studies or other contraindications to anticoagulant therapy, such hyperreaction to warfarin when administered to a patient with venous thrombosis may be an early clue to an obscure visceral carcinoma.

The finding in this case is in line with the observations of Wright.[3] He noted the absence of therapeutic effect in thrombophlebitis associated with malignancy, even though the therapeutic range was reached. He emphasized that malignancy must be suspected whenever thrombophlebitis persists or is migratory despite adequate anticoagulant therapy or whenever there is unexplained bleeding with prothrombin times in the therapeutic (not excessive) range.

The pathogenesis of multiple thrombosis in carcinoma of the pancreas and in other visceral carcinoma remains obscure. Various explanations have been offered.[7]

Gore [7b] offered an intriguing explanation for multiple thrombosis in pancreatic carcinoma. He suggested this explanation for the curious relationship between carcinoma of the pancreas and thrombosis. The key factor is functionally intact but morphologically disrupted glandular tissue as the tumor bed. The clotting disturbance stems from the release of trypsin from the disrupted glandular tissue of the tumor bed. The thromboplastic effects of trypsin ordinarily are neutralized by antitryptic substances within the serum. Their titer, as determined by measurements of plasma antithrombin, rises considerably in acute pancreatitis. However, a mechanism which operates in an acute, short-lived process may fail when the stress involving it continues over a long period. Progressive debilitation,

which occurs with cancer, increases the possibility of such failure; should it occur, the continued release of trypsin from the tumor bed would lead to intravascular coagulation. Involvement of the arterial side of the circulation, particularly of the heart valve, seems to be the only anatomic difference between this thrombotic process and the more common form of thrombosis.

The frequency with which obstructing neoplasms of the head of the gland lead to atrophy explains the lesser incidence of intravascular coagulation in that localization. Metastases within the pancreas from tumors of various origins affect the coagulative mechanism in an identical fashion. They thereby reaffirm the lack of significance of the histological type of the neoplasm in production and association of thrombosis. Malignant lesions embedded in functional pancreatic tissue cause a slow and unremittent release of trypsin into the circulation. At first, there is a compensatory rise of antitrypsin, but, over a prolonged interval marked by progressive debilitation, the antitryptic mechanism fails. This failure of the antitryptic mechanism accounts for the clotting tendency observed with the tumors of carcinoma of the pancreas.

Gore emphasized the one morphologic finding which suggests the action of an unopposed thromboplastic agent; whereas most of the thrombi are usually venous, Thompson and Rodgers found,[24] as did I, that there also is a high incidence of arterial thrombi. In several of Gore's cases of carcinoma of the tail of the pancreas with thrombosis, and in Sproul's, polypoid fibrin thrombi were attached to otherwise normal aortic or mitral valve leaflets. They were formed along the line of apposition, and their occurrence on the systemic side of the circulation, with its more forceful valvular closure, suggests that they were initiated by ordinarily innocuous endothelial injury at the site of impact. Furthermore, when circumstances favor formation of fibrin within the circulation, the motility of the leaflets provided them with a harvesting effect analogous to the action of glass beads and defibrinating blood in the laboratory. Gore explains a lowered level of prothrombin in the face of a tendency to thrombosis by the fact that the depletion is a secondary effect resulting from hyperutilization of prothrombin rather than a primary defect of its formation.

With use of warfarin, it is possible to take advantage of the early finding of a lowered level of prothrombin time in the presence of obvious thrombosis. The provocative test with warfarin is suggested as a possible useful, early diagnostic clue to the presence of a hidden or silent pancreatic malignancy, as well as malignancies in other visceral organs with possible metastases to the pancreas.

A dose of warfarin based on the weight of the patient, not to exceed a total of 75 mg., when given intravenously, intramuscularly, or by mouth, may cause the patient's prothrombin time in seconds to be so prolonged as to cause frank hemorrhage from the venipuncture site or hematuria. In my patient, 50 mg. given intravenously caused an alarming hemorrhage 12 hours after administration. The hemorrhage was later reversed by administering phytonadione. The prothrombin index 12 hours after the administration of warfarin came down to zero and remained at such a level until the administration of phytonadione. The response to vitamin K_1 indicates that there is no defect in prothrombin formation. This rebound of the prothrombin time should be considered part of the diagnostic test for prothrombin depletion.

This hyperreaction to warfarin, and possibly to its congeners, and the resistance of thrombophlebitis to anticoagulant therapy should lead the clinician to search thoroughly for a possible malignancy.[8] Such hyperreaction to warfarin when used to treat thrombophlebitis should lead the clinician to suspect carcinoma of the body or tail of the pancreas or other visceral carcinoma with metastases to the pancreas as the underlying causative factor.[1] In such an instance, an exploratory laparotomy may be indicated if all other diagnostic procedures are of no avail. When one notes such hyperreaction to warfarin administered in an initial episode of thrombophlebitis, one need not wait for further episodes of migratory thrombophlebitis before suspecting a hidden malignancy. Thus, Woolling [27] agrees with Fisher's [26] opinion that one is justified in a thorough and continuous study to rule out a developing cancer in any patient in whom at least two bona fide episodes of thrombophlebitis have occurred, regardless of the location, mildness, intensity, or duration, provided the thrombophlebitis cannot be explained convincingly on some other basis.

Prothrombin can be depleted by a relatively small dose of warfarin. Measuring each day the response of the prothrombin index to a single dose of warfarin may be a useful early diagnostic clue to the presence of cryptic visceral malignant disease. The presence of both venous and arterial thrombosis, as noted in my patient and in similar cases, would justify a suspicion of pancreatic malignancy. Thus, many months before the diagnosis of malignant visceral disease one may clinically recognize thrombophlebitis with or without the occurrence of arterial thrombosis and demonstrate the depletion of prothrombin with the aid of warfarin.

Using warfarin or its congeners for a diagnosis in a condition in which prothrombin is already depleted assumes a calculated risk of hemorrhage, on which the test resides. Hence, measures to counteract the hemorrhagic manifestations must be held in readiness. Vitamin K_1 must be on hand. Bleeding from a venipuncture site can be controlled by a pressure dressing. Hematuria can be controlled by administering 75 mg. or more of vitamin K_1 intravenously. Transfusion of fresh whole blood may be necessary.

Summary

Hyperreaction to warfarin or its congeners, when administered in a therapeutic dose to treat thrombophlebitis, should make one suspect an obscure visceral carcinoma, particularly of the body or tail of the pancreas, or other visceral carcinoma with metastases to the pancreas.

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COUNCIL ON DRUGS

Report of the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. KAUTZ, M.D., *Secretary.*

PSYCHOTHERAPEUTIC DRUGS

The introduction of a multiplicity of psychotherapeutic drugs and of new terms, such as tranquilizer, ataraxic, normalizer, calmative, neurosedative, psychic energizer, pacific, anticonfusion and antihallucinatory, creates a difficult situation for the average physician. He is confronted with the problem of evaluating claims of usefulness for a wide variety of chemical substances with diverse pharmacological effects, which are proposed for the treatment of neurotic and psychic disorders.

The terms "tranquilization" or "ataraxia" in referring to the human mental state have been variously defined, but for simplicity they can be considered to be more or less synonymous with "peace of mind." As such, they are obviously psychological rather than pharmacological terms, since the state can be produced by a multitude of drugs which either depress or stimulate the central nervous system and by others which exert only a peripheral effect on organ structures. Thus, a tranquil state can be accomplished by nonspecific sedation (alcohol, barbiturates), by analgesics (acetylsalicylic acid, morphine), by skeletal muscle relaxants (mephenesin, meprobamate), by autonomic suppressants (chlorpromazine, reserpine), and by many others. "Peace of mind" can also be created in depressed individuals by the judicious use of substances that are pharmacological stimulants, such as amphetamine. In the broadest sense, therefore, the reversal of any clinical disorder, even by drugs with only peripheral effects (epinephrine in asthma and digitalis in cardiac decompensation), can result in "peace of mind" by relieving anxiety. This concept is the fundamental basis of psychosomatic medicine.

From a practical point of view the time has long since passed when it would be useful, or even possible, to attempt to establish the designation "tranquilizer" or even "specific tranquilizer" as a pharmacological term that could be considered synonymous with what might be termed "autonomic suppression." Likewise, it is no longer feasible to limit the application of such a term to particular

substances, such as chlorpromazine and reserpine, whose introduction into psychotherapeutic practice, because of unique pharmacological properties, created the present dilemma. Indeed, it appears probable that the gradually increasing number of new drugs, as well as new terms, will add to rather than detract from the confusion in this important field.

It seems wise to bear in mind that regardless of terminology, the ideal objective of psychotherapy with drugs is to induce an improved mental state, irrespective of what subjective symptom or objective sign is being treated. This should be done with agents that produce no undesirable subjective responses, are lacking in toxic side actions, and exert no summative effects with other drugs unless the latter are beneficial.

In accordance with the foregoing considerations, the Council has voted to abandon the section on Ataraxics in New and Nonofficial Drugs and to describe agents proposed for use for their particular effects on the central nervous system, in accordance with their fundamental pharmacological classification, insofar as this is known. On the basis of present knowledge, the drugs in this general category can be classified under the following headings:

I. Antihistamines
  A. Psychotherapeutic antihistamines
    a. Hydroxyzine (Atarax) hydrochloride
II. Central Nervous System Depressants
  A. Nonselective Depressants
    1. Analgesics
    2. General anesthetics
    3. Hypnotics and sedatives
  B. Selective Depressants
    1. Anticonvulsants
    2. Antihistamines (as above)
    3. Antitussives
    4. Central muscle relaxants (skeletal muscle relaxants), nonsedative
      a. Mephenesin (Avosyl, Dioloxol, Kinavosyl, Lissephen, Mephenesin, Mepherol, Mephson, Myoten, Myoxane, Oranixon, Prolax, Saserol, Sinan, Spasmolyn, Tolansin, Tolosate, Toloxyn, Tolserol, Tolulox, Tolyspaz)
      b. Mephenesin carbamate (Tolseram)
    5. Central muscle relaxants (skeletal muscle relaxants), sedative
      a. Meprobamate (Equanil, Miltown)
      b. Phenaglycodol (Ultran)
      c. Promoxolane (Dimethylane)
    6. Central parasympathetic suppressants
      a. Benactyzine (Suavitil) hydrochloride
    7. Central sympathetic suppressants, phenothiazine derivatives
      a. Chlorpromazine (Thorazine) hydrochloride
      b. Mepazine (Pacatal) hydrochloride
      c. Perphenazine (Trilafon) hydrochloride
      d. Prochlorperazine (Compazine) maleate
      e. Promazine (Sparine) hydrochloride
      f. Triflupromazine (Vesprin) hydrochloride
    8. Central sympathetic suppressants, rauwolfia derivatives
      a. Alseroxylon (Rauwiloid)
      b. Deserpidine (Harmonyl)
      c. Rauwolfia (Raudixin, Rauserpa)
      d. Rescinnamine (Moderil)
      e. Reserpine (Rauloydin, Raurine, Reserpine, Reserpoid, Roxinoid, Sandril, Serpasil, Serpiloid)
III. Central Nervous System Stimulants
  a. Methylphenidate (Ritalin) hydrochloride
  b. Pipradrol (Meratran) hydrochloride
IV. Miscellaneous Agents
  a. Azacyclonol (Frenquel) hydrochloride

CHEMICAL LABORATORY

The Chemical Laboratory has authorized publication of the following statement.

WALTER WOLMAN, PH.D., *Director.*

Monographs of tests and assays for new and nonofficial drugs adopted by the Chemical Laboratory of the American Medical Association represent an expression of opinion as to what might constitute adequate tests and assays to serve as a reference guide to those interested in the identity and quality of a new and nonofficial drug.

Completed monographs are published in the journal *Drug Standards* for those interested in the details of the procedures. Monographs on the following drugs have appeared in the November-December, 1957, issue of that journal. The cooperation of the listed pharmaceutical firms that furnished samples and data is acknowledged.

Busulfan ..... (Burroughs Wellcome & Co., Inc.)
Cryptenamine ..... (Irwin, Neisler & Co.)
Cryptenamine acetates ..... (Irwin, Neisler & Co.)
Cryptenamine tannates ..... (Irwin, Neisler & Co.)
Isometheptene ..... (Knoll Pharmaceutical Co.)
Isometheptene hydrochloride ..... (Knoll Pharmaceutical Co.)
Isometheptene mucate ..... (Knoll Pharmaceutical Co.)
Tridihexethyl iodide ..... (Lederle Laboratories)

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FAT EMULSION FOR INTRAVENOUS USE

GUEST EDITORIAL

Warren H. Cole, M.D.

FOR MANY years the medical profession has been searching for a stable nontoxic fat emulsion which when given intravenously to patients would be assimilated for caloric use. The need for such an agent is greatest in patients who are malnourished and who, for one reason or another, are unable to take food by mouth. Surgical patients fall into this category more often than others, since oral feedings are interrupted by every celiotomy, and often oral intake is not possible for several days thereafter. The greatest usefulness for such an agent would be in malnourished patients having an abdominal disease needing surgical correction, but in whom the lesion is of a type not permitting sufficient oral intake to convert the operative risk from poor, or fair, to good. These lesions are numerous indeed, and include patients having carcinoma of the gastrointestinal tract, ulcerative colitis, regional enteritis and many others. The November issue of *Metabolism: Clinical and Experimental* contains 23 papers (from 22 different institutions) dealing entirely with a newly developed fat emulsion (Lipomul) which appears to meet the requirements searched for. These papers deal with numerous aspects of the emulsion, including particularly the preparation, utilization, and reactions. In addition, at the end is a summary or discussion in which all reactions or possible deleterious effects are brought up for consideration by all present at the symposium (held at Brook Lodge, Augusta, Mich., May 21 and 22, 1957, under the auspices of the Upjohn Company). Numerous investigators during the past three or four decades have prepared fat emulsions of various types, but, up to the present, reactions after their injection have been too severe to allow general use. The reactions sustained by injection of the present emulsion are so mild that apparently all of the investigators reporting were willing to continue using the product on a clinical basis.

From the Department of Surgery, University of Illinois College of Medicine, Chicago.

The emulsion is made from a highly refined cottonseed oil. Soya phosphatide (lecithin) was used as the emulsifying agent, as in previous investigations, but the serious reactions experienced previously have been prevented by removing a certain objectionable fraction from the phosphatide. Utilizing a coemulsifying agent (a polyoxyethylenoxypropylene polymer), the manufacturers have been able to reduce sharply the amount of phosphatide needed to stabilize the emulsion. The actual constituents are cottonseed oil, 15 Gm.; Phosphatides (purified soya lecithin), 1.2 Gm.; polyoxyethyleneoxypropylene polymer, 0.3 Gm.; dextrose, 4.0 Gm.; and water for injection, up to 100 ml. The dextrose is added to obtain isotonicity. The fat globules are predominantly 0.5 to 1 μ in diameter; not over 0.02% of the visible particles are larger than 1.5 μ in diameter. Vigorous shaking for 72 hours at 5 C does not produce any change in the size of the particles; it is stable for at least one year if stored in a refrigerator. At the present time the emulsion is put up in bottles containing 500 cc. (15% fat), with a nutritional value of approximately 800 calories.

As stated, the various investigators reporting in this symposium studied innumerable characteristics of the emulsion. In the discussion held at the end of the symposium all present were invited to comment on the various characteristics discussed. All those studying the ulilization of the injected fat seemed convinced it was utilized completely or nearly so and that the emulsion had a prominent protein-sparing effect. Dosage is obviously an important item. Many investigators reported 1,200 cc., and some even up to 1,800 cc. per day without untoward reactions other than the persistence of lipemic serum. The speed of injection is relatively unimportant, but very few infusions have been given faster than 5 cc. per minute. Accordingly, it was agreed that, if a severe nutritional deficiency were present, at least two bottles might safely be given per day. Many of the investigators had given as many as several hundred injections; often 30 or 40 were given to the same patient. There were no

fatal reactions, and in fact few indeed which were serious; the very few serious reactions (e. g., hepatomegaly, purpura) occurred only after extended therapy of daily injections for several weeks.

Numerous subjective complaints such as headache, backache, and anorexia were reported, but they were so infrequent and so mild that they were not considered significant. One investigator reported an increase in the blood pressure level after administration of the emulsion, but, since this will occur after intravenous administration of glucose, blood, and many other such agents, it was agreed this response was insignificant. Occasionally pyrexia was produced, however, no one reported any deleterious effects of this reaction; moreover, when the emulsion was given later these patients usually had no pyrexial reaction. Minor changes in sulfobromophthalein and thymol readings were reported, due presumably to fat in the Kupffer's cells; this reaction was not considered significant, particularly since it was very transient. The emulsion produces little or no local reaction when extravasation occurs; numerous investigators reported no ill-effects from this complication. One of the essayists reported that an increased coagulability of the blood was noted during the time patients are lipemic, but no one observed any tendency for production of thrombophlebitis or pulmonary embolism.

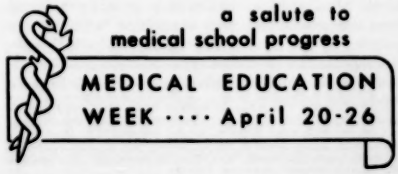
In the final discussion or summary, the moderator attempted to find out if the investigators present could agree on contraindications. There appeared to be practically no contraindications, except that all would agree that if a reaction were sustained the injection should be stopped. If daily injections for many days or weeks were followed by untoward reactions, the injections should obviously be discontinued. Hypertension, hepatic disease, jaundice, and fever were discussed as possible contraindications. However, it was agreed that such conditions are not contraindications, although the precautions taken during any intravenous injection should be followed. Slow clearance of the fat in the serum was reported by several essayists. Although no explanation of this phenomenon was made, it was agreed that the emulsion should be given cautiously in such cases, and in moderate amounts daily.

In conclusion, it appears that practically all, if not all, investigators present at the symposium considered the emulsion in its present form to be safe for clinical use, and to be utilized by the patient. The long-continued search for an emulsion of intravenous fat for clinical use may be at an end. Such an agent will be very useful indeed in treating undernourished patients who can take little or nothing by mouth. The surgeon will probably profit most from this agent, because improvement in physical reserve is so often necessary before operation can be performed safely, and so often such patients can take very little by mouth. It should be just as valuable in postoperative treatment when adequate oral intake is prevented by one reason or another.

This material is available at present only on an investigational basis, but it is hoped that a product of this type will be available through the usual channels in the very near future.

THE "YOUNGING" OF ELECTORATES

The never-ending struggle of physicians with disease sometimes creates the impression that each hard-won gain will eventually mean an increasing proportion of older adults. Nevertheless, as the article beginning on page 1051 points out, the proportion of older adults in some nations will soon start to decline despite the phenomenal medical progress of recent decades. Meanwhile, more and more persons will enjoy the privilege of dying old instead of dying young. But this privilege will not result in a topsided age distribution of adults in several Western nations. Starting in 1961 in Australia the aging of the electorate will give way to the "younging" of the electorate. The proportion of adults aged 50 and over will start declining in New Zealand in 1962, in France in 1965, and in the United States in 1970. The author, the director of the Bureau of Medical Economic Research of the American Medical Association, analyzes the influence of the age factor on certain trends in Western countries, particularly in Australia and New Zealand, where he conducted his study during the first four months of last year. His conclusion that the era of aging electorates will soon terminate into a new era of younging electorates provides the medical profession and the American people with a new insight into some of the great social, political, and economic crosscurrents of the third quarter of the 20th century.



ORGANIZATION SECTION

OLD-AGE AND SURVIVORS INSURANCE DISABILITY PROGRAM

Committee on Medical Rating of Physical Impairment

One of the tasks of the Board of Trustees' Committee on Medical Rating of Physical Impairment is to keep the medical profession informed on developments concerning the medical aspects of the disability provisions in the Old-Age and Survivors Insurance (OASI) section of the Social Security Act. A complete description of this program, prepared in question and answer form by the Committee, was published in the June 1, 1957, issue of THE JOURNAL, pages 566-571. Reprints of the article were distributed on June 28, 1957, to all constituent associations with notice of the following action by the House of Delegates.

At the 1957 Annual Meeting of the American Medical Association, the House of Delegates adopted a recommendation by the Committee on Medical Rating of Physical Impairment and the Board of Trustees that each constituent medical association appoint a committee whose principal objectives and activities should be (1) the promotion of mutual understanding and effective relationships between local administrative agencies and the medical profession, (2) the provision of technical advice and consultation regarding medical aspects of local administration of Public Law 880; and (3) the development of educational material for publication in state medical association journals and bulletins and distribution to individual physicians.

It was also suggested that each constituent medical association offer the services of such a "medical advisory committee" to regional representatives of the Bureau of Old-Age and Survivors Insurance and to state administrative agencies. (A list of state administrative agencies and their medical personnel appears at the conclusion of this report.) The designation "medical advisory committee" has, unfortunately, caused some confusion at the state level. Most state administrative agencies have at least one official "advisory committee" which is appointed by the head of the agency and which may have physician members. The interests and activities of such an official advisory committee to state agencies are not necessarily those of a committee appointed by a constituent association. The former represents the state governmental agency; the latter represents the practicing profession.

It is, therefore, important for each constituent association to authorize a committee to actively implement the objectives outlined above. In connection with such a committee's activities, the Committee on Medical Rating of Physical Impairment wishes to remind constituent associations that determinations of disability under this program are administrative decisions as to whether an applicant is or is not disabled, including the date of onset or cessation of disability. These determinations are solely the responsibility and function of the administrative agency and are not an appropriate function of individual physicians or a committee of a constituent association. The following report on consultative examinations, however, suggests the type of activity in which state medical association committees should engage.

Members of the Committee on Medical Rating of Physical Impairment are Raymond M. McKeown, Chairman, Coos Bay, Ore.; George F. Gsell, Wichita, Kan.; Henry H. Kessler, Newark, N. J.; Quentin W. Mack, Boise, Idaho; James R. McVay, Kansas City, Mo.; O. A. Sander, Milwaukee; and Mr. George W. Cooley, Secretary, and Mrs. Marjorie W. Grigsby, Research Associate, Chicago.

Consultative Examinations Under the OASI Disability Program

The Committee on Medical Rating of Physical Impairment wishes to call the attention of constituent associations to the substantial increase in consultative examinations being purchased with federal funds by the state agencies administering the Old-Age and Survivors Insurance disability program. During the 15-month period following July 1, 1956, state agencies reported to the Bureau of Old-Age and Survivors Insurance that 26,958 consultative examinations had been authorized at a total cost of $626,000.

Between July 1 and Sept. 30, 1956, only 287 consultative examinations, involving 0.9% of the total cases disposed of during that period, were reported by state agencies. The average cost per examination was $22.64.

Between July 1 and Sept. 30, 1957, however, 13,165 consultative examinations, involving 15.8% of the total cases disposed of during that period, were reported by state agencies. The average cost per examination was $22.60.

It is the responsibility of a state agency to decide what medical evidence is needed and the best source of such evidence. However it should be noted that for every one consultative examination required in the third quarter of 1956, there were 49 consultative examinations required in the same quarter one year later. This denotes a trend with

implications which deserve prompt study by constituent associations and full discussion with state medical consultants and review physicians. In doing so the following facts should be kept in mind.

An applicant under the OASI disability program is required by law to obtain, at his own expense, sufficient medical evidence from which a determination of his case can reasonably be made by the state agency review team composed of a physician and an individual qualified to assess the work history, occupational capacity, and other important factors. This medical evidence must support the applicant's claim as to both the onset of disability and his present condition. Individual medical examinations, records, and other data the applicant needs to prove his disability may not be paid for from OASI funds.

After the applicant has submitted sufficient medical evidence to show there is a reasonable likelihood that his impairment is severe enough to qualify him as disabled, consultative examinations may be authorized and paid for from OASI funds if there is some question as to whether a sound decision can be made.

The state agency medical consultant or review physician decides when a consultative examination is necessary, who is to make it, and the type and scope of the examination. A consultative examination may vary from a simple laboratory test to a complete medical examination, including work evaluation and a complete diagnostic examination. Hospitalization for observation and tests, but not for treatment, may also be authorized.

In selecting the physician to make the consultative examination, the state medical consultant or review physician is expected to conform to the customary practice of the state agency or to follow the procedure he believes most suitable to local conditions and consistent with noninterference in the doctor-patient relationship. The medical policies and practices of the state agency depend on the relationship between the agency and the medical profession at the state level. The degree of participation by the applicant's physician in selecting the consultant to whom his patient is referred depends upon the policy of the state agency. The state agency may adopt a policy that the physician making the consultative examination must be mutually acceptable to the applicant's physician and the medical personnel of the state agency. In at least one state, the medical personnel of the state agency do not designate the consulting physician but allow the applicant's physician to refer his patient to the physician's usual consultant in the given type of case.

Consultative examinations may be authorized for the following purposes:

1. Verifying the medical proof of disability that the applicant has submitted personally or through his physician. It is obvious that a consultative examination may be necessary when the applicant is appealing from an original determination of his claim or in the occasional case where verification of the medical proof is necessary and can be accomplished only through a consultative examination.

2. Providing additional medical details to confirm the diagnosis or establish the severity of the applicant's present condition, including measurement of his remaining functional capacities or the potential remediability of the condition. The majority of consultative examinations appear to be authorized for this purpose.

Presumably consultative examinations are authorized because they are necessary. How many of these consultative examinations for each of the above purposes are in fact necessary and the reasons therefore require careful study in each state by the constituent association committee concerned with this program. Some of the questions which may be useful in studying this problem are:

1. An applicant is required by law to initiate and support his claim by obtaining, at his own expense, sufficient medical evidence from which a determination of his claim can reasonably be made. Are consultative examinations being authorized when (*a*) He does not do so at his own expense? (*b*) He cannot do so at his own expense?

2. If so, what factors contribute to this modification of legal requirements? Administrative problems or practices? Lack of cooperation by the applicant's physician? The applicant's lack of cooperation or of financial resources necessary to obtain the data required?

3. What proportion of consultative examinations are authorized because the applicant's physician does not report in sufficient detail on the history, symptomatology, clinical findings, and diagnosis so that another physician can establish the degree of severity of the applicant's impairment from the data provided?

4. In what type of cases and in what respects are the medical reports by the applicant's physician inadequate for determination purposes?

5. What proportion of consultative examinations are authorized because the state medical consultant or review physician requires a wide range and variety of medical data in order to arrive at a decision in the case?

6. What are the state medical consultant's or review physician's reasons for considering the medical evidence insufficient as submitted by the applicant or his physician?

7. What proportion of consultative examinations are authorized as the result of the Bureau of Old-Age and Survivors Insurance requesting the state agency to reconsider the case because (*a*) The Bureau does not agree with the state agency determination? (*b*) The applicant is dissatisfied with the determination in his case?

8. The applicant's physician may be authorized by the state agency to develop, at government expense, additional medical data needed to confirm the diagnosis or severity of the applicant's condition, i. e., serve as a consultative examiner. When the medical evidence is considered insufficient by the state agency physician, what efforts are made to enlist the services of the applicant's physician in developing the additional medical data needed?

STATE AGENCIES UNDER AGREEMENT TO MAKE DISABILITY DETERMINATIONS PURSUANT TO SECTION 221 OF THE SOCIAL SECURITY ACT

Note: Where two agencies are shown the second agency prepares determinations on disabilities involving blindness. The physicians listed under each state agency are the state medical consultants and reviewing physicians participating in OASI disability program as listed by the Bureau of Old-Age and Survivors Insurance in November, 1957.

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NATIONAL CONFERENCE ON RURAL HEALTH

The Council on Rural Health of the American Medical Association will hold its 13th National Conference on Rural Health, March 6-8, at Hotel Heidelberg, Jackson, Miss. The sessions will be attended by physicians, nurses, representatives of farm organizations, and governmental agencies. The program follows:

THURSDAY MORNING, MARCH 6

CARLL S. MUNDY, M.D., *Presiding*

8:00 **Registration**

9:45 OPENING SERVICE
Community Singing
INGRID THERESE
Associate State 4-H Club Leader, State College, Mississippi

10:00 **Invocation**
DR. W. DOUGLAS HUDGINS
Pastor First Baptist Church, Jackson, Miss.
GREETINGS
THE HONORABLE J. P. COLEMAN
Governor of the State of Mississippi, Jackson, Miss.
THE HONORABLE ALLEN C. THOMPSON
Mayor of the City of Jackson, Jackson, Miss.
GEORGE M. FISTER, M.D.
Liaison Member, Board of Trustees, American Medical Association, Ogden, Utah
HOWARD A. NELSON, M. D.
President Mississippi State Medical Association, Greenwood, Miss.
CHARLES R. HENRY, M.D.
Regional Director Council on Rural Health, Little Rock, Ark.

10:50 **As the World Turns**
F. S. CROCKETT, M.D.
Chairman, Council on Rural Health, American Medical Association, Lafayette, Ind.

11:10 **A New Look at Our Changing Rural Society**
A. F. WILDEN, Ph.D.
Professor of Rural Sociology, University of Wisconsin, Madison, Wis.

DISCUSSION LEADER
J. P. SCHMIDT, Ph.D.
Extension Professor, Agricultural Extension Service, Ohio State University, Columbus, Ohio

THURSDAY AFTERNOON

CHARLES R. HENRY, M.D., *Presiding*

2:00 COMMUNITY SINGING

2:05 **Some Nutritional Target Areas as the World Turns**

Presentation
H. H. ALP
Director, Market Development, American Farm Bureau Federation, Chicago
RUTH M. LEVERTON, Ph.D.
Assistant Chief, Human Nutrition Research Board, Agricultural Research Service, U. S. Department of Agriculture, Washington, D. C.
DICK K. CASON, M.D.
Hillsboro, Texas
JANET L. CAMERON
Food and Nutrition Specialist, Agricultural Extension Service, Virginia Polytechnic Institute, Blacksburg, Va.
MIRIAM G. EADS
Extension Specialist in Nutrition, Agricultural Extension Service, Purdue University, Lafayette, Ind.
4-H Girl—MISS HELEN GAYLE TURRENTINE
Davidson County, Tenn.
4-H Boy—RODNEY HENDERSON
Mississippi State College, State College, Miss.

3:40 **Family Visit to the Dentist**
CLAUDE S. WILLIAMS JR., M.D., D.D.S.
Hattiesburg, Miss.
Family from Hinds County, Mississippi

THURSDAY EVENING

W. J. WEESE, M.D., *Presiding*

8:15 **A Visit to Your Physician**
WYATT NORVELL, M.D.
New Castle, Ky.
MRS. ANN CORLEY
Nurse, Jackson, Miss.
ALMA McMASTERS
Technician, Jackson, Miss.

FRIDAY MORNING, MARCH 7

NORMAN H. GARDNER, M.D., *Presiding*

9:00 COMMUNITY SINGING

9:05 **Safety Panel**
DAN REED
Osceola, Ark.
W. L. WILSON, M.D.
Director, Division of Occupational Health, Texas State Department of Health, Austin, Texas
HUGH A. MATTHEWS, M.D.
Canton, N. C.
SGT. CHARLES ALLENDUFF
Director, Crash Injury Research, Indiana State Police, Indianapolis
MAYNARD COE
Director, Farm Division, National Safety Council, Chicago

11:00 **What the Patient Expects of the Doctor—What the Doctor Expects of the Patient**
MRS. WILLIAM WILKIE
Widener, Ark.
MRS. HOMER GREENE
Tutwiler, Miss.
PAUL NICKERSON, M.D.
Sylacauga, Ala.
J. L. WALKER, M.D.
Clarksville, Ga.

FRIDAY AFTERNOON

FRED A. HUMPHREY, M.D., *Presiding*

1:30 COMMUNITY SINGING

1:35 **Changing Patterns Affecting the Cost of Health Services**
TOM J. HITCH
President, Tennessee Farm Bureau Federation, Columbia, Tenn.
AMOS N. JOHNSON, M.D.
Garland, N. C.
JOHN F. MODRALL
Director Employee Communications and Public Relations, Eli Lilly and Company, Indianapolis
O. W. BEELER
Rural Enrollment Counselor, Blue Cross—Blue Shield, Chicago
HOWARD BROWER
Assistant Secretary, Council on Medical Service, American Medical Association, Chicago

2:10 **Physician Distribution: The Dynamic Dilemma**
GEORGE E. TWENTE, M.D.
Jackson, Miss.

FRIDAY EVENING
F. S. CROCKETT, M.D., *Presiding*

7:00 BANQUET
Invocation
MOST REVEREND JOSEPH B. BRUNINI, D.D.
Auxiliary Bishop of Natchez, Jackson, Miss.

INTRODUCTION OF SPECIAL GUESTS
Greetings
MRS. PAUL C. CRAIG
President, Woman's Auxiliary, American Medical Association, Wyomissing, Penn.
ROBERT RAKEL
President, Student American Medical Association, University of Cincinnati, Cincinnati

MUSICAL INTERLUDE
Medicine's Prestige
HOWARD A. NELSON, M.D.
President, Mississippi State Medical Association, Greenwood, Miss.

Patient-Physician Cooperation in Rural Health
F. J. L. BLASINGAME, M.D.
General Manager, American Medical Association, Chicago

SATURDAY MORNING, MARCH 8
W. WYAN WASHBURN, M.D., *Presiding*

9:00 COMMUNITY SINGING

9:05 **We Work for Health**
MRS. JOHN RICE
President, Illinois Health Improvement Association, Sheldon, Ill.

9:30 **Something Old: Something New**
MRS. FRANCES H. MACDONALD, R.N.
Director, Visiting Nurses Association, Oklahoma City, Okla.

10:00 **The Fourth "H"**
PAUL M. BANCROFT, M.D.
Lincoln, Neb.

10:35 **There's a Right Way**
Method Demonstration Team
FREDDIE LEWIS
RAY SULLIVAN JR.
Hinds County, Miss.

11:00 **Preceptorship Program in Ohio**
ROBERT E. REIHELD, M.D.
Orrville, Ohio

11:30 **It's Your Move**
MRS. CHARLES W. SEWELL
Member-at-Large, Advisory Committee, Council on Rural Health, Otterbein, Ind.

PLAN SAN ANTONIO MEDICAL SCHOOL

The Council on Medical Education and Hospitals has accepted with "recommendatory action" a survey report which notes that "San Antonio offers a favorable milieu for the location of a medical school."

A summary of last October's survey, conducted at the request of the Texas Commission on Higher Education, was presented to the A. M. A. Council at a recent meeting in Philadelphia. The survey team of Drs. Joseph C. Hinsey, J. Murray Kinsman (both representing the Association of American Medical Colleges), W. Clarke Wescoe, and James M. Faulkner (representing the Council on Medical Education and Hospitals) reported: "It is significant that the local medical profession, both individually and collectively, have been working energetically for the establishment of a medical school in San Antonio. The team was impressed by the high caliber of the profession in San Antonio and feels that it could play an indispensable role in a clinical teaching program."

Title to 160 acres of land on the outskirts of the city already has been acquired by leading citizens organized as the San Antonio Medical Foundation—with the view of establishing a new medical school there. Such a school would also benefit by an offer of the Bexar County Medical Society to make its excellent library available for student and faculty use. Potential for clinical teaching exists in three general hospitals, a tuberculosis and a mental hospital operated by the state, and in plans for a Methodist hospital adjacent to the proposed medical school site.

Nearby medically related facilities include the Southwest Foundation for Research and Education, the Air Force School of Aviation Medicine, Lackland Air Force Base Hospital, the Army Medical Service School, and Brooke Army Hospital and its surgical research unit.

The survey team stated that final decision for a medical school in San Antonio "will necessarily be determined" by citizen needs in Texas and by ability to provide sufficient funds for support. Further discussion of the survey was scheduled before the Council at its meeting in Chicago. At its meeting in Philadelphia last December, the Council also:

—Assigned to its Committee on Preparation for General Practice the task of considering a plan to establish a special board of family physicians.

—Named Drs. Faulkner, Warde B. Allan, and Harlan English to a joint committee with representatives of the AAMC—with the mission of blueprinting medical education's role in time of national emergency. They are to initiate a broad plan of how best to prepare for such "castastrophe" eventualities as student selection and military deferment, medical school relocation, program acceleration possibilities, internship and residency training, and faculty problems. The joint committee already has established liaison with the A. M. A. Council on National Defense.

—Voted to confer with the AAMC on the prospect of developing a statement on the functions and structure of two-year medical science programs, along the lines of an already-developed "Functions and Structure of a Modern Medical School."

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BUREAU OF MEDICAL ECONOMIC RESEARCH

THE "YOUNGING" OF ELECTORATES

Frank G. Dickinson, Ph.D.

As the bumper crop of babies born since World War II matures into 21-year-old voters, the electorates of Western nations will start "younging." The proportion of older voters, which has risen rapidly in the 20th century, will reach a peak and then decline. The terrific pressure on political leaders to provide security for the rising tide of oldsters—and, perhaps, to advance other welfare state programs—will wane. The accent will again be on youth, as one of the great forces which produced the trend toward the welfare state goes into reverse gear.

Consider voters 50 years of age and over as the older voters and those below age 50 as the younger voters. How soon will the percentage of older voters start to decline in some of the leading Western nations? The table shows the peak year and the shift in the number of older voters per 100 voters since about 1910 for five selected countries.

Australia will lead the parade of nations into the era of the younging electorate starting in 1961. New Zealand will be a close second. Strangely, France will have third position in this parade with a very high, flat peak of 45% in 1965. The proportion of older voters in the United States will not hit its peak of 40% until 1970, but the decline thereafter will be quite rapid. If we do not look beyond 1978, the turning point (of at least 47%) for Great Britain is not in sight.

Peak Year and Peak Percentage of Older Voters and Shift per 100 Voters Since 1910 for Five Selected Countries

	Peak Year	Peak % of Older Voters	Increase per 100 Voters Since 1910
Australia	1961	39 to 39.5	15
New Zealand	1962	38	15
France	1965	45	10*
United States	1970	40	15*
Great Britain	after 1978	47+	20* and still rising

* Since women did not obtain the franchise in the United States, France, and Great Britain until after 1910, they are excluded from the percentage of older voters for that year. Except for Australia, the above percentages refer to the proportion of older adults—approximately the same as the proportion of older voters.

Four Months Down Under

I spent the first four months of 1957 in Australia and New Zealand, primarily because they will be the first nations to end this era of the aging electorate. There were other reasons. Unlike federal elections in the United States, 90 to 95% of those who can vote, do vote. Hence the age distribution of those who actually vote in these two countries is almost the same as the known age distribution of those who are eligible to vote. The proportion of younger voters and older voters who stay at home on election day is insignificant. On the other hand, the trend toward the welfare state began earlier in these two countries than in the United States. The applicability of observations regarding them to the United States must, of course, be approached with great caution. This is especially true of New Zealand, where many of the 2¼ million inhabitants take pride in thinking of their country as the foremost laboratory for social experimentation.

Another reason for spending four months "down under" was to find the answers to a puzzling question. What social, economic, and political changes resulted from an increasing proportion of older adults? In the case of Australia how extensive was the impact of the shift of 15 votes a 100 in a half-century from the younger to the older group? The economists I interviewed were not as helpful as I had expected; the professors of history and political science provided perspective. But I got my real help from the clergy and the outstanding political leaders of both New Zealand and Australia.

The clergy must look at the whole of life—birth, marriage, and death. The passing of time is more meaningful to them because they deal with the old and the young. I asked the priests, the bishops, and the archbishops of the Anglican and Catholic churches in Australia what changes in the work of the clergy had resulted from the fact that the older half of the people who died in 1900 had lived at least 34 years, whereas the older half of the people who died in 1956 had lived at least 68 years. First, they were shocked by my question and asked proof for the statement, which I had verified at the Bureau of the Census in Canberra. Australia was in the forefront of nations which early in this century enjoyed reduced maternal and infant mortality. The entire health record of the people of Australia (and New Zealand), who sprang largely from hardy Britishers with the yen to migrate, has been outstanding. They were justifiably proud of that fine health record. We talked of the declines in the death rates from contagious diseases and other younger causes of death. Having established the basic fact,

Director, Bureau of Medical Economic Research.

the interviews developed many indications of the powerful forces set in motion in Australia during the past half-century by the aging of the population, or, if you will, by the privilege of dying old instead of dying young. Indeed, these thoughtful clergymen agreed that the privilege of dying old was the genius of the 20th century and likely to become its unique contribution to the long history of mankind.

The Rhythm of Life

One Anglican bishop, who had been a boy of 16 in the Australian bush in 1900, claimed that he could still wield an axe with great accuracy for a few minutes. He spoke of the tragedy of dying young in the back country from accident or disease at the turn of the century.

So the younger half of those who died in Australia in 1900 had lived 34 years or less. I can remember funerals for many young men and for young mothers who died in childbirth. The community felt the tragedy deeply and resented this interruption in the rhythmic course of life. Sometimes there was a definite feeling of rebellion against Providence for allowing such things to happen, and so often. My feeling is that as the years have gone on in Australia and the typical age at death has become so much greater, death is now regarded as a more normal part of the procedures of life. It fits into the scheme of nature—spring, summer, autumn, and winter. While there is inevitable grief, that grief is not long sustained and it is not felt disloyal to the deceased if it is not sustained. Nowadays death falls into its natural place in the economy of life and nature.

Yes, Dr. Dickinson, dying old instead of dying young has produced an acceptance of death instead of a rebellion against it. And, as an old woodsman, I observe that the agony of dying has been greatly reduced by drugs and one hears today many fewer stories of the grim agonies of those on the death bed. Clergymen conducting a funeral for a man aged 68, and at other times, stress that religion is now more concerned with living, whereas in my youth religion was more concerned with dying. So were the hymns we sang. From the minds of youth in Australia the fear of dying young has largely disappeared except for an early death from violence. In Australia, concern with the prospects of living too long has largely taken the place of the pre-World War I fear of dying young.

A Catholic archbishop stressed another aspect of dying old.

Some persons are more aware of death. Good practicing Catholics who say a number of Hail Mary's each day ('now and at the hour of our death') should be more aware than others of the rising average age at death. In general, I think that the deeper appreciation of death has decreased in the past several decades. Moreover, the aging of the electorate has contributed to the development of the welfare state which is somewhat more advanced in Australia than in other British countries, except New Zealand. I have noticed over the years that the strongest advocates of the welfare state, particularly those seeking higher pensions, were older persons.

A young Presbyterian clergyman stressed another angle.

Young people today do think less frequently about death except during wartimes. As a result they think they can postpone thinking seriously about religion for another 10 or 15 years. As the fear of imminent death from disease is reduced, the need to make religious decisions one way or the other is lessened. The privilege of dying old encourages procrastination about religious convictions. I was ordained only 10 years ago. So I have not witnessed this shift in the median age at death from age 34 to age 68 since 1900. I am glad that I live in an era when death typically comes so late in life and seems more natural. Preaching a funeral service for a young person today is a very depressing experience for me. A funeral sermon for an older person, say one aged 68 or over, involves far less emotional strain for me and for the relatives, neighbors, and friends.

Two Other Causes

The historical reductions in mortality at the younger ages, dying old, or longer life is not the sole explanation of the aging of the electorate in Australia or any other country. The two additional factors are (1) great fluctuations in the annual birth rate (and in the number of births) and (2) immigration or emigration. The 21st year after a year of relatively few births becomes a year in which the number of persons attaining voting age is reduced accordingly; likewise, 21 years after a large number of births the number of new voters will be great. Because of the low birth rate in Australia during the depression of the 1930's, the number of new native voters attaining age 21 in the late 1950's has been relatively small. For example, the number of new 21-year-old voters in 1955 derived from the babies born in Australia during 1934 was below normal. So some of the shift from younger voters to older voters during the 1950's was due to the fewness of births during the 1930's and not to longer life.

Under the new immigration policy sponsored by the Rt. Hon. Arthur A. Calwell of the Labor party soon after World War II, Australia has been receiving a large number of young immigrants. These young Europeans have, so to speak, taken the places of the babies not born in Australia between the two world wars and have smoothed out the age distribution of the population. About 42,000 of 100,000 new Australians each year are 20 to 34 years of age as compared with only 23% of the Australian-born population. Admitting 100,000 immigrants each year into a country with fewer than 10 million inhabitants is comparable to the Melting Pot period in the United States of a half-century ago. Then, as now, the people who pull up stakes and leave their country are mostly young workers and are, on the whole, probably somewhat more vigorous than the population which they left.

Without this new immigration policy Australia would not be the first nation to turn the political-demographic corner. As a matter of fact, the proportion of adults aged 50 and over in Australia will not hit its peak of 37.1% until 1966 as contrasted with the peak of 39 or 39.5% of older voters in 1961. The reasons for this lag of five years are the requirement of five years' residence for new Australians of non-British origin and, secondly, their

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tardiness in becoming citizens as soon as possible. In particular, the large number of new Australians from Italy, Poland, and the Netherlands must wait five years to be naturalized and many of them who arrived seven or eight years ago are still not citizens of Australia. Those of British origin can vote six months after arrival. This naturalization requirement was not important during the period of low immigration prior to World War II, when more than 90% of the immigrants came from Great Britain and the Commonwealth countries. In the post-World War II immigration, the level has been much higher than pre-war, but the proportion of British origin has dropped below 50%.

Three Unequal Factors

Even a cursory analysis of the relative importance of each of these three factors on the age distribution of adults in each of the five countries is far beyond the scope of this article. The older voters were born at least half a century ago; hence any attempt to assay the influence of fluctuations in the annual number of births would require a review of annual births from about 1880 onward. For example, the birth rate was not high in France at the turn of the century. But all five countries experienced declines in the birth rate during the 1930's. On the other hand, the influence of reducing mortality is somewhat less diverse than the fluctuations in births among the five countries; New Zealand and Australia, however, led in reducing mortality.

No generalizations can be made about the third factor, migration, as it has varied so much among the five countries during this century. It has been a major factor since World War II in Australia. The migration to New Zealand of British subjects has exerted a small but rather steady influence there. In 1921-1923 the United States suddenly shut off the immigration spigot which had tended to keep the adult population young. Those who came to the United States as young workers before 1921 are now a third of a century older and they are not being counterbalanced by a large number of young immigrants today. The end of the period of the aging of the adult population of the United States would come before 1970 if the United States had adopted a post-World War II immigration policy similar to that of Australia.

Although Great Britain has received a considerable number of immigrants during the past decade, the large number of young people who have left to take up homes in Australia and Canada has aged the British electorate.

Since our data deal only with adults, the effect of steadily lowering the mortality among infants and children produces only a secondary effect, a later increase in the number of adults per 1,000 babies. In the case of France, the annual number of births since 1900 has been so low that the age distribution of adults had begun to approach some kind of a normal pattern prior to the rise of the birth rate after World War II. Indeed, the mortality gains at the younger ages during this century in the Western nations has almost run its course. The new lower mortality pattern among persons under 40 or 50 years of age will be subject to only modest improvements in the coming decades. A glorious era in mortality is ending. The problem now is to maintain and slightly increase the gains at the younger ages and to reduce the mortality at ages 50 and over from cancer and heart diseases. I hope some day to measure these three forces separately, although it would involve a rather detailed demographic history of each of the five countries.

Population Projections

How can one speak with any degree of confidence about the age distribution of adults or voters in 1960 or 1970? In fixing the turning points which mark the end of the period of the aging of the adult population or voters and the beginning of the new period of the younging of the adult population or voters, I have used published and unpublished population projections prepared by an agency of each of the five governments. These data can be used with some degree of confidence if one stops at 1978. No speculation about future birth rates is involved. All of the children who will attain age 21 by 1978 are already born; they have been counted. The number of children who will die before attaining age 21 can be rather safely predicted on the basis of mortality experience. Admittedly a substantial decrease in cancer and heart disease mortality among older voters could postpone the turning points a few years in each country.

The only other forecast deals with the number who will continue to reside in the country of their birth and the remainder who will migrate to another country. In these official population forecasts it was necessary for me to make some choice of estimates of the annual number of immigrants and emigrants to be expected in each year between now and 1978. Only for Australia was my selection very important; I chose to use the population projections based upon the assumption of 100,000 immigrants a year. Even if this number should be reduced substantially between now and 1965, the onrush toward voting age of the large number of young children born since World War II would probably be sufficient to maintain 1961 as the turning point; the decline in the proportion of older voters thereafter would be less rapid. The proportion of new Australians aged 21 and over who could be expected to be naturalized citizens in each future year did involve some speculation on my part. Some of the differences between the predicted age distribution of adults and of voters may, in retrospect, prove to be in error. Five years from now these projections of the age distribution of adults can be extended

to 1983 without speculating about the number of births in each of the next five years. To do so now seems too hazardous.

Looking Backward

The increase in the number of older voters per 100 voters between 1910 and the peak years will be 15 in Australia, 15 in New Zealand, 15 in the United States, 10 in France, and at least 20 in Great Britain. To what extent has this shift from younger voters to older voters in each country been responsible for the trend toward the welfare state in the intervening decades? I put this question to a dozen leaders of public opinion in New Zealand and threescore leaders in Australia during the first four months of last year. I recorded more than 75,000 words of these interviews. This poll was not of the man-on-the-street type, nor was it of a scientifically selected sample of all the people of the two countries. It was a poll of mature leaders; only two of them were under 35 years of age. I agreed not to quote them directly without their consent, but a summary of their interpretations of the role of the aging of their electorates on the political, economic, and social history of their countries since 1910 is very illuminating.

A Shift of Fifteen Votes

The first response of experienced political leaders to my questions regarding the role played by this shift since 1910 of 15 votes a 100 from the younger to the older group was usually another question: "Don't you mean, Dr. Dickinson, a shift of five votes or two votes a 100 instead of 15? In a close election campaign a shift of one vote per 100 can be decisive. A veteran of many political campaigns can hardly comprehend a shift of 15 votes." But when they realized this shift had taken place slowly during a half-century, they could place the question in true perspective.

One out of 10 political leaders interviewed stated flatly that such a slow-moving force was obviously extremely weak and that it was difficult to assign to it any political events of recent decades. The other nine agreed that it was one of the most powerful influences in New Zealand and Australian politics during the half-century. I found that most of them were not familiar with the statistics but were keenly aware of the shift. They count the political pulse by their mail and by observing the ever-increasing proportion of older faces in their campaign audiences.

A one-question response to my query was very incisive, and even more significant because it was voiced by the Rt. Hon. Robert G. Menzies, who has been Prime Minister of Australia longer than any of his predecessors. I asked him if he would care to comment on the opinion other political leaders had given me that the aging of the electorate had greatly influenced legislation during the past few decades. He replied, "Isn't that what we mean by democracy?"

A large increase in any group of voters in a democracy is likely to be manifested in legislation reflecting the interests and aspirations of that group. Several political leaders pointed to the acceptance by the Liberal (conservative) party, when it came to power in 1949, of the old-age pension program developed earlier by the Labor party. A professor of political science noted that the Liberal party had never decreased pension benefits but the Labor party, in a less favorable economic period, had reduced them. He also suggested that the acquiescence of the Menzies government in the old-age pension program had its counterpart in the United States in 1954 when President Eisenhower persuaded the Congress to increase greatly the monthly amount of old-age pension benefits through amendments to the Social Security Act which had been inaugurated 19 years earlier by the Democratic party.

Several political leaders suggested that I interview a certain man who had served many years as an employe of the Federal Parliament. They told me that this man would give me the "low-down" on the real motives of the members of Parliament in supporting or opposing important pieces of legislation during his period of service. After describing some of the personal traits of a considerable number of the great and near great leaders of Parliament during the past quarter-century he said:

> I suppose that political leaders in my country have much in common with those in your country. They want to be re-elected. They put their best foot forward and in public statements give only the best reasons for supporting or opposing certain legislation. In that sense, they are like salesmen or advertising men.
>
> I have listened to them in the cloakrooms of Parliament and drunk thousands of cups of tea with them. The reasons given in private for their support or opposition to certain bills were often very different from the reasons they gave the public. I don't think the less of them for that. But I can tell you that for a good many years members of the Federal Parliament have been harassed by groups pleading the case of the older voter for pensions. Don't let anyone tell you that the aging of our electorate has not been a powerful political force because I know many political leaders in all parties have felt it necessary to yield to the wishes of the older voters. The older voter has been in the saddle many years without having a party of his own.

I was surprised that some political leaders during interviews preferred not to use the term welfare state even though they knew it was coined by British, not American, economists. Thereafter, I began to use the term social insurance, which is more specific. In most social insurance programs among the nations of the world one-half to two-thirds of the tax money or benefits involved is for old-age pensions. Pensions are the financial cornerstone of social security systems. Some leaders also called attention to the fact that recent increases in old-age

pensions had been considerably greater in Australia than the increases in maternal welfare benefits, a payment to parents at the younger childbearing ages.

There is a provision in the constitution of Australia, adopted in 1901 when it became an independent nation, specifically authorizing the federal government to enact laws providing for old-age pensions. Pension laws had been developed earlier in the states of Victoria and New South Wales. Two historians I interviewed expressed the view that these earlier state pension laws were completely disassociated from the development of social security legislation in the 1930's and should be considered an inevitable result of economic, social, and political developments in Australia in the 1870's and 1880's. That is, these early state pension systems were in no way related to the aging or the younging of the electorate but sprang from other Australian developments in the late 19th century. As one economist put it:

> The holiday from principal political attention to social services from 1912 to 1941 is partly attributable to national concern with other more pressing matters. We were trying to become a nation. The labor unions were so concerned with wages set by our special arbitration courts that pension legislation was slighted. World War I created many problems for us. The relative stability of prices during the 1920's lulled us. Some students claim that Australia ceased to be a social pioneer in 1914. It was not until 1947 that a unified nationwide social security system was established. It may well be that your idea about the aging of the electorate had something to do with this long dry spell in social legislation. Certainly the proportion of older voters increased during those three decades. I confess that I have not considered such demographic factors.
>
> Democracy works in fits and spurts. The only people who could lose their savings under the depressed conditions of the 1930's, were, of course, those who had savings. They were the older people. Some of our students of social security developments in Australia would even say that we had no comprehensive system until 1947. At any rate these major developments must be credited to the Labor party.

After 1961

So much for the present and the past. The period of the aging of the electorate will soon end. How will the younging of the electorate affect social, political, and economic developments in Australia? Admittedly the corner will be turned very slowly, and it might well be described as a very smooth bend rather than a corner. The new trend will be a wobbly force hedged in by other forces. The shifting of these 15 votes a 100 from the older group back to the younger group will come slowly; and it is not now possible to predict how soon the older portion of the electorate will decline from the peak of about 39% back to the 1910 level of 24%. When the record of births, deaths, and immigration in Australia for the 1960's is completed it may be possible to select that future year. Certainly the change-over in 1961 and during the balance of the 1960's will be more negative than positive; it will be the effect of the older proportion of voters no longer rising rather than the impact of a decline. Yet it seemed worthwhile to ask these leaders of opinion to speculate with me about the changes in Australia that might come after 1961.

As might be expected, their opinions differed greatly. Most of those who thought the aging of the electorate had been an unimportant factor in recent decades also minimized the potential impact of the younging of the electorate. Without exception, they regarded the prospect of a younging electorate as "good news" for Australia. On balance, the persons interviewed agreed that there would be less stress on pensions and other special benefits for older voters, although their number would be rising. A clear majority of them thought that the older political leaders were more radical because many of them were steeped in the socialistic ideas so prevalent before World War I. Almost every person interviewed called attention to the lack of perspective and understanding of persons under 30 years of age, who were too young to appreciate the problems created by the depression in the 1930's. They were too young to know the meaning of debt, bankruptcy, unemployment, and bread lines. As teenagers and later as young adults they had lived in an expanding economy.

Even the most devoted members of the Labor party whom I interviewed agreed that the young voters were simply not interested in the radical ideas which had stimulated so many young crusaders in the era before World War I. These young voters are much more interested in schools, good roads, and good housing than in the class struggle between the bourgeoisie and the proletariat. They seem to be more absorbed in local than in international issues, with two exceptions. The enormous concentration of communists in southeast Asia and China seems like the sword of Damocles. The second worry springs from the first—their concern with the grave potentiality of atomic and nuclear warfare, from which Australia would not be isolated.

New Australians

A thoughtful journalist diverted the discussion to the new Australians. He contended that they are not a cross section of the population from which they came as to age or personal initiative. He pointed to some of these people in his own community who held two jobs, built half a house, and lived in it until they saved up enough money to complete the other half.

> What chance has socialism in a country infiltrated by these vigorous young people from Europe who want to become individual enterprisers as soon as possible after they arrive. Many of them fled to escape communism. I expect that the taxi driver who brought you to my home this evening spoke with an Italian or Polish or Dutch accent. He probably works eight hours at some other job. Some Labor party leaders now advocate a reduction of immigration from Europe but favor an increase in the number from

Great Britain as the latter are more likely to have socialistic leanings. Since so many of the young voters after 1961 are going to be these vigorous New Australians, the rising tide of young voters will create an economic drive the likes of which we have not seen in Australia for decades. In summary, the results of the younging of the electorate are going to be much greater than they would have been if this expanding group of new voters had all been native Australians. Before the New Australians started to come in large numbers in 1949, I am afraid we had become a bit lazy. They are revitalizing our nation.

A New Zealander's Forecast

In this brief sketch New Zealand has been neglected. It is a land of green grass, rather rugged terrain, and friendly people. The Southern Alps of the South Island form one of the beauty spots of the world. Perhaps the outstanding feature of the economy is the efficient, commercial dairy in which one man can take care of 60 milk cows. This world-renowned efficiency is due in a large measure to the abundance of grass throughout the year, which saves much time for the dairyman. New Zealand exports dairy and meat products and must import many manufactured products, automobiles, and petroleum products to maintain a good standard of living. The economists and other leaders I visited thought that it would be very difficult for their country to achieve success through industrialization. A bare majority of them seemed content with the welfare state which has proceeded much further in New Zealand than in Australia. An elder statesman of New Zealand told me:

> I have been in political life for a long time. The older voters have dominated both parties. The young profited by our inflation, the old by pensions. Thus far no major blow-up over taxation has developed. If the younging of the electorate proceeds far enough in New Zealand, the democratic process will bring the younger voters to a position of dominance in both political parties. But I don't know exactly what the younger voters will want then. A scientific opinion poll today would not indicate these future differences. During the transition decade, it may be politically wise to increase government largess to both the young and old voters. The great change will come after my time. But young men entering politics today should expect to serve the younger voters first. Otherwise we shall have a revolt of youth, like the revolt of women in your country which eventually gave them the right to vote.

Watch Australia

Australia, the dry empty continent, is still dry but not quite so empty. Although its area is the same as that of the United States, the 10 million inhabitants are concentrated along the eastern and southern seaboard. Steel is abundant and its cost of production is only two-thirds of the cost in the United States. Australia lacks petroleum. Its need for water in the great open spaces is even greater. There are some who hope that cheap atomic power, which does not involve electric lines or other transportation, may solve part of the water problem for vast areas.

I found the people of Australia midway between the extremely pro-British New Zealanders and our own industrial-minded Americans. They want to become an industrial nation. They want the population to increase as rapidly as possible. The bombing of Darwin in northern Australia by the Japanese during World War II had a tremendous psychological impact. It marked the end of their era of splendid isolation from the rest of the world. Many of those I interviewed felt certain that the high tide of socialism was passed in 1948 when the proposal to nationalize the banks by the Labor party was responsible for its defeat.

For many years there has been a considerable variety of proposals to create a compulsory contributory pension system to replace the present non-contributory system based on a means test. One astute political leader expressed the hope that if this should come to pass Australia would not make the mistake the United States and other nations have made. He said:

> It is obviously unfair to have the same rate of contribution for older workers who will contribute only a few years. An increase in public pension benefits is like starting a new pension system. The equitable way is to make the contribution rate higher for those who are going to contribute fewer months, say those over age 50. This fits in with your notion that we are approaching an era when the proportion of younger voters will increase. They will certainly question unfair taxation. We must be sure to treat them fairly, and a system of step-rate contributions for old-age pensions will do just that. Then, a younging electorate might not threaten the pension system.

Perhaps Australia ceased to be a social pioneer in 1914. Since the younging of electorates will start there first, Australia may regain its pre-World War I status in the next 10 to 15 years.

An Era Ends

A series of interviews in one of the state capitals of Australia further clarified the forces being examined. One leader said:

> I like your selection of age 50 as the dividing line between younger and older voters. Age 65 is much too high. I turned age 50 a few years ago. Like other families with parents in our age class, our children are now grown; and the older ones have left home. We no longer have the expense of feeding and clothing them and paying for their education. We have finished paying off the mortgage on our home. In a word, my wife and I are now looking West. We are concerned with the very real prospect, in this era of low mortality, of living on into retirement. We have intense interest in all kinds of pension proposals. One could say that when we turned 50 we became pension-conscious.

Only one thing is certain about social evolution—every stage comes to an end. During the past half-century, there is much evidence that the influence of older voters on legislation has been greater than their number merited, because the proportion of them was rising. As we look beyond the problems of providing schools for the large number of youngsters and think of them as adults later on, it should

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be clear even to those who are unfamiliar with population projections that young voters will be quite numerous in a decade or so. Then the political leaders will want to please the younger voters at every turn. Although the absolute number of older voters will continue to increase, the drive which their expanding numbers developed in the past half-century for welfare state programs, anchored on free or almost free public pensions, will wane.

There are other powerful forces at work in New Zealand, Australia, and the United States, as well as in France and Great Britain. Among these are mass production, urbanization, a steady rise in the level of education, mechanization of the home, much more travel, nuclear power. The younging of the electorate—one force among many—will, I believe, put a brake on the trend toward the welfare state and lessen the clamor for the guaranteed future, the riskless society. No one should attempt to circumscribe the future, especially its capacity for social innovation. Moreover, we must all admit that prophecy is still an exclusively divine gift. Yet, the vigor of younging electorates should be unquestioned and anticipated.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

Postgraduate Courses

Notices of the following courses have not previously been published by the Council and are presented for information only:

The **Fifth Annual Symposia in Medicine** will be presented Tuesday evenings, 8-10 p.m., for six weeks beginning April 1 at the Fort Miley Veterans Administration Hospital, 42nd Avenue and Clement Street, San Francisco, in cooperation with the San Francisco Academy of General Practice, Stanford University School of Medicine, and the University of California School of Medicine. This 12-hour course, though designed primarily for physicians in general practice, is open to physicians who are not members of the Academy as well as to hospital resident staffs.

The home study courses in **electrocardiography** by the University of Southern California School of Medicine, listed on Aug. 17 in THE JOURNAL will be offered again beginning March 26, 1958. Inquiry should be addressed to the Director, Postgraduate Division, University of Southern California School of Medicine, 2025 Zonal Ave., Los Angeles 33.

The American College of Physicians has scheduled the following courses, in cooperation with the institution named: **Methods of Auscultation in Cardiac Diagnosis,** a 3-day, 20-hour course, at New York University–Bellevue Medical Center, April 10-12; **Cardiovascular Disease,** a 5-day, 35-hour lecture course at the American College of Physicians' headquarters, April 14-18; **Current Views in the Diagnosis and Treatment of Cardiovascular Diseases,** a 5-day, 40-hour lecture, panel, and open question period course at the University of Illinois College of Medicine, Chicago, May 12-16; **Principles and Practice of Internal Medicine,** a 5-day, 35-hour lecture, seminar, and open question period course at the State University of Iowa College of Medicine, June 2-6; **Selected Topics in Hematology for Internists,** a 5-day, 40-hour laboratory, lecture, panel, and open question period course at the University of Rochester School of Medicine and Dentistry, June 9-13, 1958. All courses are designed primarily for specialists in internal medicine. All have a fee of $30 for American College of Physicians members and $60 for nonmembers. Inquiries should be addressed to Registrar, American College of Physicians, 4200 Pine St., Philadelphia 4.

A one-day symposium, **Arthritis—Practical Considerations in Diagnosis and Management,** is scheduled for March 5 at the University of California at Los Angeles Medical Center. Further information may be obtained from Assistant Dean for Postgraduate Medical Education, UCLA Medical Center, Los Angeles 24.

An intensive, continuous four-week course, **Principles and Techniques of Tissue Culture,** will be given July 7-Aug. 1 at the University of Colorado School of Medicine, Denver. The lecture, demonstration, discussion, and laboratory work course, sponsored by the Tissue Culture Association, is designed for postdoctoral workers (M.D. or Ph.D.) who plan to use cultured tissues in teaching or research. Requests for application forms should be addressed to Dr. Mary S. Parshley, Columbia University College of Physicians and Surgeons, 630 W. 168th Street, New York 32, sufficiently in advance that they may be completed and returned by May 1.

A postgraduate course, **Surgical Anatomy,** is scheduled May 26-June 21, 1958, by Cornell University Medical College. The full-time, five and a half day a week course will consist of an intensive review of surgical anatomy, with demonstrations and dissection, at a tuition of $200. It will be especially designed for physicians in specialty training for surgery, with enrollment limited to 25. Inquiries may be directed to the Office of the Dean, Cornell University Medical College, 1300 York Ave., New York 21.

MEDICAL NEWS

CALIFORNIA

Gift for Children's Wing at Medical Center.—A gift of 1.5 million dollars for construction of a new children's wing of the University of California Medical Center, Los Angeles, has been presented by Marion Davies, former screen star. The new four-to-six-story construction will be a southeast wing of the medical center extending from the present outpatient department. Dr. John M. Adams, chairman, pediatrics department, will direct activities in the new wing. The first floor will house the Children's Clinic which Miss Davies established in 1933, and in 1952 the university School of Medicine assumed its operation.

Society News.—The Los Angeles Surgical Society has announced the election of Dr. O. Dale Lloyd as president and Dr. James F. Regan as secretary-treasurer, for 1958.——The San Francisco Medical Society has installed the following officers: Drs. Claude P. Callaway, president-elect; Robert C. Combs, president; Dorothy P. Danno, vice-president; Roberta F. Fenlon, secretary; George K. Herzog Jr., treasurer; and Edgar Wayburn, editor.——The California Society of Internal Medicine has installed the following officers: president, Dr. Robert L. Smith Jr., San Francisco; vice-president, Dr. Walter P. Martin, Long Beach; secretary-treasurer, Dr. Clyde C. Greene Jr., San Francisco. The next annual meeting will be held Oct. 17-19 at Yosemite Valley.——At a recent meeting of the Los Angeles Society of Allergy the following officers were elected for 1958: Dr. Jerome J. Sievers, president; Dr. Ralph Bookman, vice-president; and Dr. Isadore Pitesky, secretary-treasurer.

DISTRICT OF COLUMBIA

Forum on Medical Economics.—Six area societies making up the District Medical Council will sponsor an all-day forum, "The Doctor and His Practice," on current problems in medical economics in cooperation with The William S. Merrell Company at the Hotel Statler March 27. The forum chairman is Dr. Henry H. Ferrell Jr., Alexandria, Va., vice-president of the council. The program will cover three basic subjects: (1) The Doctor and his Office, (2) The Doctor and the Law, (3) The Doctor and his Life Planning. Physicians attending the forum will have the privilege of calling on any speaker for personal help and referral with specific medical economics problems. Dr. Howard A. Rusk, director of the department of physical medicine and rehabilitation, New York University–Bellevue Medical Center and associate editor, the New York *Times*, will speak at the luncheon on "Stress in the World, the Individual and the Doctor." Other speakers include Ernest Dichter, New York; Carl Holzheimer, Chicago; C. Joseph Stetler, Chicago; James A. Eubanks, New York; George W. Condit, New York; R. Crawford Morris, Cleveland; Robert B. Murphy, Madison, Wis.; Amiel Caplan, estate planning authority; and Bernard D. Hirsh, Chicago. A report will be given by Mr. Stetler on the results of a survey concerning medical professional liability which the A. M. A.'s Law Department has completed.

ILLINOIS

Chicago

Nutrition Lecture.—Dr. Thomas R. C. Sisson, department of pediatrics, University of Rochester School of Medicine and Dentistry, Rochester, N. Y., will discuss "Iron Metabolism of Pregnancy and the Newborn" at a luncheon meeting of the Chicago Nutrition Association, March 5, in the Georgian Room, Carson, Pirie, Scott and Company. Information may be obtained from C. Edith Weir, President, Chicago Nutrition Association, 939 E. 57th St., Chicago 37.

Hospital News.—The sixth lecture in the eighth annual North Shore Hospital lecture series on "The Emotional Problems of Childhood" will be held March 5, 8 p. m. "Management of Social Adjustment and Behavior Problems in Adolescence" will be discussed by Dr. Joseph B. Cramer, director of child psychiatry, Albert Einstein College of Medicine, New York City, and director of child psychiatry, Bronx Municipal Hospital Center. The Commission on Education of the American Academy of General Practice has approved these lectures for category II credit.

Annual Clinical Conference.—The Chicago Medical Society's annual clinical conference will be held March 4-7 at the Palmer House. About 35 papers are scheduled for presentation, and four luncheon round-table discussions are planned. Dr. Walter C. MacKenzie, chairman, department of surgery, University of Alberta Faculty of Medicine, Edmonton, Canada, will present "A 'New Look' at Diverticuli-

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

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tis" March 4. A panel discussion on tranquilizing drugs is arranged for March 6, with Dr. Jacob E. Finesinger, Baltimore, as moderator. Clinics on osseous trauma, medical color telecasts, and scientific and technical exhibits are arranged. A special program is planned for the ladies. Registration fee for nonmembers is $5. For information write The Chicago Medical Society, 86 E. Randolph St., Chicago 1.

INDIANA

Dr. King Honored.—Dr. William F. King, State Health Commissioner from 1922 to 1933 and Indiana State Board of Health staff member from 1910 to 1954, recently received a bronze plaque from the American Nursing Home Association "in recognition of his outstanding contributions in the field of gerontology." Dr. King reportedly was instrumental in bringing about the establishment of a division within the Board of Health which concerns itself with problems of advanced years. In 1945 he was appointed head of the Division of Gerontology and Chronic Diseases and served as director of this division until 1949 when he went on a consultant status.

KANSAS

Orthopedic Surgery Laboratory Completed.—The James B. Weaver Laboratory for Orthopedic Surgery has been completed in the orthopedic section, University of Kansas School of Medicine, Kansas City. The laboratory is a memorial to the physician who was on the faculty of the School of Medicine for 30 years, the last 10 years as head of the section of orthopedic surgery, prior to his death April 30, 1956. The new facility is a laboratory for clinical chemistry and it will be used for research in orthopedics. It contains the "bone bank," a project founded and used extensively by Dr. Weaver. Dr. Weaver worked with the Kansas Crippled Children Commission for 30 years, and for three years was a member of the commission's board. He was influential in planning the Children's Rehabilitation Center, now under construction at the Medical Center. The initial research to be carried on in the laboratory will be directed by Dr. Leonard F. Peltier, professor of surgery and successor to Dr. Weaver as head of the orthopedic section. It will be directed in the field of fat embolism.

MARYLAND

Dr. Woods to Receive Gonin Medal.—Dr. Alan C. Woods, emeritus professor of ophthalmology, Johns Hopkins University School of Medicine, Baltimore, has been named to receive the Gonin Medal of the University of Lausanne, Switzerland, and the Swiss Ophthalmological Society at the International Congress of Ophthalmology to be held in Brussels, Belgium, in September. The medal was instituted in 1937 jointly by the university and the society to honor the memory of Jules Gonin, professor of ophthalmology at the university, who established the pathogenesis of detachment of the retina and devised the fundamental operation. The International Council of Ophthalmology was designated to select the recipient once every four years. The recipient is invited to the University of Lausanne to make a short address at a preliminary function. Dr. Woods will attend such a function July 12. Awarded the American Medical Association's Ophthalmological Research Medal in 1948, Dr. Woods began teaching in ophthalmology at Johns Hopkins in 1919. He is an honorary fellow of the Royal College of Surgeons (Edinburgh), a member of the American Ophthalmological Society (vice-president, 1954; received the Howe Research Medal, 1953), and a member of the American Academy of Ophthalmology and Otolaryngology (president, 1947).

MISSOURI

Thompson Lectureship.—Dr. LeMoyne Snyder, Paradise, Calif., has been chosen to present the ninth annual Dr. F. G. Thompson Sr. Lectureship April 24 by the Thompson–Brumm–Knepper Clinic, St. Joseph. Dr. Snyder's subject will be "Murder Challenges the Doctor."

MONTANA

Dr. Slaughter to Give Cancer Lecture.—The first Mary E. Swift Memorial Cancer Lecture, "Debatable Problems in Cancer," will be presented by Dr. Danley P. Slaughter, chairman, Cancer Committee, American College of Surgeons, March 8 in Butte at the banquet of the Mary E. Swift Foundation and Tumor Registry and Clinic. Preceding the lecture, informal rounds and a tumor clinic will be conducted at St. James Hospital. Attendance is limited to physicians. For reservations (fee for banquet $6.50) write to the Mary E. Swift Tumor Registry, Silver and Idaho Streets, Butte, Mont.

NEW YORK

Close Broadacres Sanatorium.—The State Health Department has notified the Oneida County Board of Supervisors that the Broadacres Sanatorium, Utica, will be returned to Oneida County. Transfer of patients from the Broadacres District to the Homer Folks Tuberculosis Hospital at Oneonta began in February and will be completed in April. Dr. Hilleboe said a period of several months will be required for relocation of employees, inventory of equipment and supplies, and transfer of records. The State Health Department will return the equivalent of equipment and supplies in the hospital which were present at the time the depart-

ment acquired the property from the county in 1948. In 1957, the State Health Department recommended to the budget director that Onondaga Sanatorium at Syracuse be closed. Shortly thereafter the Oneida County Board of Supervisors requested that Broadacres Sanatorium be returned for use as a chronic disease hospital. The State Health Department gave priority to the request of Oneida County officials. Oneida county officials plan to use the hospital for the care and rehabilitation of the chronically ill.

New York City

Hospital News.—Dr. Joseph W. Beard, professor of surgery, Duke University School of Medicine, Durham, N. C., will present "Tumor Viruses" March 7 as part of the schedule of lectures by the Division of Neoplastic Diseases at Montefiore Hospital.

Symposium on Tay-Sachs' Disease.—A Symposium on Tay-Sachs' Disease will be held April 10, 9:30 a. m., at the Isaac Albert Research Institute of the Jewish Chronic Disease Hospital, Brooklyn. This meeting will be under the joint auspices of the Albert Einstein College of Medicine of Yeshiva University and the National Tay-Sachs' Association. Dr. Ernst Klenk, of Cologne, Germany, will be among the participants. Interested persons are invited. For information write the Jewish Chronic Disease Hospital, East 49th Street and Rutland Road, Brooklyn 3.

Project for Blind Children.—The Blind Children's Research Project for the emotionally disturbed and multiple handicapped will become a service of New York University-Bellevue Medical Center's Institute of Physical Medicine and Rehabilitation with the beginning of the spring semester. Initiated two and a half years ago at the School of Education by the Association for the Advancement of Blind Children, an organization made up of parents of blind children and interested professional people, the project is devoted to "creating better understanding of the blind child with special problems." Under the direction of Virginia Mae Axline, Ed.D., associate professor of education at the university, and the medical supervision of Dr. George G. Deaver, director of the Children's Division at the Institute of Physical Medicine and Rehabilitation, the services offered consist of play therapy and counseling for children and their parents, research, advanced professional training, and public education. The Blind Children's Research Project relies completely on the support of voluntary contributions. Estimated budget for full professional staff and equipment is $50,000 to $75,000 a year.

School for the Mentally Retarded.—Plans for a new school for the mentally retarded at West Seneca have been announced jointly by Dr. Paul H. Hoch, commissioner of mental hygiene, and John W. Johnson, superintendent of public works. Cost of the project is estimated at 50 million dollars. The new school will serve the counties of Erie, Niagara, Orleans, Genesee, Wyoming, Allegany, Cattauraugus, and Chautauqua. Patients from those counties are now being received at Newark. Mentally retarded persons of all ages will be accepted for care, training, and treatment at the school. Designed for 2,400 patients, the institution will be provided with service facilities for future expansion to accommodate 3,000. Initial construction will include facilities for about 1,700 patients. Patients' accommodations will consist of 30-bed cottages for educable boys and girls of school age. Buildings for adult patients will house 120 patients in four wards of 30 beds each. Buildings for severely retarded patients, many of whom will be physically handicapped, will provide for 130 patients each, divided into three 40-bed wards and an additional 10-bed ward for patients requiring temporary medical care for acute illnesses. The medical program of the institution will be centered in the medical-surgical building for about 200 patients. There will also be a physical rehabilitation building. Another building for 180 infants and young children will be erected in the medical treatment area. A children's psychiatric hospital, a self-contained unit for emotionally disturbed children, will accommodate 200 children in separate cottages of 25 patients each, attached to a central corridor connected with its own school, gymnasium, and auditorium and an administrative area for staff and treatment offices.

NORTH CAROLINA

Cancer Symposium in Winston-Salem.—The seventh annual cancer symposium, sponsored by the Forsyth County Medical Society in cooperation with the Forsyth Cancer Service will be held April 10 at the Hotel Robert E. Lee, Winston-Salem. The following guest speakers will participate: Dr. Ralph Jones Jr., professor of medicine, The University of Florida, Miami; Dr. James F. Holland, hematologist, Roswell Park Memorial Institute, Buffalo, N. Y.; Dr. James E. Lofstrom, radiologist, Detroit Memorial Hospital, Detroit; Dr. Charles L. Spurr, professor of medicine, Bowman Gray School of Medicine, Winston-Salem. The program has been entitled "Recent Advances in Chemotherapy of Leukemias and Lymphomas." Open discussion will follow the formal presentations. For information write Dr. William H. Boyce, chairman, Forsyth Cancer Committee, Wake Forest College, The Bowman Gray School of Medicine, Winston-Salem, N. C.

Grants for Study of Psychological Stress.—A Duke University Medical Center research team working under provisions of two U. S. Public Health Service grants that total $51,100 has begun studying bodily

reactions to various psychological stresses. Principal investigators are Dr. Albert J. Silverman, director, Duke psychiatry department's psychophysiology laboratory, and Dr. Sanford I. Cohen, associate director of the laboratory. A grant of $36,100 from the National Institute of Mental Health has been made to support an investigation of the relationships that exist between emotions and various bodily changes. This work is being done in association with Dr. McChesney Goodall Jr., associate professor of surgery at Duke and a specialist in the study of body hormones that include those under investigation. A second grant of $15,000 came from the National Institutes of Health funds awarded to Duke University last summer for the support of a Regional Center for the Study of Aging.

PENNSYLVANIA

Another Amendment to Radiation Protection Regulation.—Dr. Charles L. Wilbar Jr., state secretary of health, has announced that the State Advisory Health Board has approved an amendment to Radiation Protection Regulation 433 requiring the use of aluminum filters, cones, and diaphragms on diagnostic x-ray and fluoroscopy machines. The regulation, administered by the State Health Department's Division of Industrial Hygiene, is "designed to protect the public against dangers of ionizing radiation and was originally adopted by the Advisory Health Board on Oct. 20, 1956." The amendment reads:

Amendment to Radiation Protection Regulation 433 Diagnostic Uses of X-rays

a. The total filter—permanently in the useful beam—shall be equal to at least 2½ millimeters of aluminum on all x-ray machines capable of operating at or above 60 kilovolts peak when used for routine diagnostic x-rays or routine diagnostic fluoroscopy.

b. The primary x-ray beam for routine diagnostic x-rays or routine diagnostic fluoroscopy shall not be larger than clinically necessary. Cones and diaphragms shall be used to limit the area of the primary beam.

This is the second major amendment to the Radiation Protection Regulation 433. In February, 1957, an amendment was adopted, outlawing shoe-fitting fluoroscopes.

Appoint Dr. Cheever Dean at Pittsburgh.—The appointment of Dr. Francis S. Cheever as dean of the University of Pittsburgh School of Medicine has been announced. Dr. Cheever will assume his new duties in the School of Medicine July 1, succeeding Dr. William S. McEllroy who is retiring but will continue as a special adviser to the chancellor on medical affairs. Since 1950 Dr. Cheever has been professor of microbiology in the Pitt Graduate School of Public Health. Before joining the Pitt faculty, he was assistant professor in the Harvard Medical School from 1946 to 1950 and an instructor from 1938-1941. He was on duty with the U. S. Navy from 1941 to 1946 and in 1944 and 1945 was director of the Enteric Pathogen Laboratory of the U. S. Naval Medical Research Unit on Guam, Okinawa, and the Philippines area. Since 1951 he has served as special consultant to the Communicable Disease Center of the U. S. Public Health Service.

New Allegheny County Hospital.—The new Allegheny County Hospital, eight miles from downtown Pittsburgh, was dedicated Feb. 7. The 22-million dollar structure which stands on a 126-acre plateau will provide beds for 2,100 patients. Six years in planning and three years in building, it comprises a main hospital building of eight stories, two convalescent wings of three stories each, two rows of ambulatory dormitories ringing a park-like area, an auditorium, interdenominational church, power station, separate nurses' homes, and eight physicians' residences. The hospital kitchen is equipped to serve 10,000 meals a day, and the laundry can handle 15,000 pounds of wash a day. Other facilities include a recreation program, library, canteen, and

The new Allegheny County Hospital, with the main eight-story building (right), the convalescent section (left), ambulatory wards (extending out of view at left), and the pyramid-like interdenominational church (left center).

a beauty and barber shop. The hospital will function under the board of commissioners of Allegheny County, Mr. John J. Kane, chairman. Dr. Gerard P. Hammill, director of the Allegheny County Institution District, is medical director of the hospital.

Philadelphia

University News.—Dr. Y. Ikemi, associate professor of internal medicine, Fukuoka University, Japan, now at the Temple University Medical Center as a visiting fellow in medicine, spoke before the staff and faculty recently on "Experimental Studies on Psychosomatic Aspects of Diseases of Internal Medicine."

UTAH

Surgeons Meeting in Salt Lake City.—A three-day sectional meeting of the American College of Surgeons will be held in Salt Lake City March 17-19 at the Hotel Utah. Dr. Alfred M. Okelberry, associate clinical professor of orthopedic surgery, University of Utah School of Medicine, is chairman of the advisory committee on local arrangements. Topics will include pediatric surgery, post-traumatic

paraplegia, trauma, cancer, ACTH and cortisone in surgery, common-duct stones, cardiac resuscitation, bleeding peptic ulcer, hand surgery, and a full day in ophthalmic surgery. Medical motion pictures will also be shown. An innovation at this year's sectional meeting is the fellowship luncheon, featuring a panel discussion on college activities, with a question period. Dr. Ezekiel R. Dumke, Ogden, will preside, and Dr. Hubbard P. Saunders, associate director of the college, will serve as moderator.

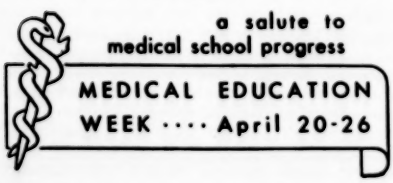
GENERAL

Medical Faculty Awards.—The Lederle Laboratories Division, American Cyanamid Company, has announced 18 recipients for its Medical Faculty awards, intended for "strengthening the preclinical departments of medical schools in the U. S. and Canada by contributing to the support of the teaching and research activities of members of such departments who already have demonstrated high quality of performance but who have not yet attained permanent faculty tenure."

Southeastern Surgical Congress in Baltimore.—The 26th annual assembly of the Southeastern Surgical Congress will be held March 10-13 at the Lord Baltimore Hotel, Baltimore. About 53 papers are scheduled for presentation, including those of the following guest speakers: Drs. Charles W. Mayo, Rochester, Minn.; J. Garrott Allen, Chicago; Bentley P. Colcock, Boston; Hayes Martin, New York City; Charles C. Lund, Boston; Donald A. Covalt, New York City; Samuel P. Harbison, Pittsburgh; Robert R. Smith and James R. Jude, Bethesda, Md.; E. Lee Strohl, Chicago; John M. Beal Jr., New York City; George P. Rosemond and Isidor S. Ravdin, Philadelphia; and Donald R. Webster, Montreal, Canada. Four panel discussions are planned:

Diverticulitis of the Colon, moderated by Dr. Mayo.
Tumors of the Neck, moderated by Dr. Martin.
Pre- and Postoperative Care, moderated by Dr. Willard H. Parsons.
Gastric Ulcers, moderated by Dr. Ravdin.

For information write Dr. Benjamin T. Beasley, Secretary-Director General, The Southeastern Surgical Congress, 701 Hurt Building, Atlanta 3, Ga.



Physicians Among "Ten Outstanding Young Men."—The U. S. Junior Chamber of Commerce has named four physicians among the 10 men selected as "outstanding Young Men of America for 1957." The physicians are:

Dr. Thomas G. Baffes, Skokie, Ill., "developer of a surgical correction for transposition of the great vessels of the heart."
Dr. Richard A. Dewall, Minneapolis, "developer of a simplified mechanical heart-lung machine."
Dr. Robert E. L. Nesbitt Jr., Albany, N. Y., "researcher in cause and prevention of infant death in association with the birth process.
Major David G. Simons, M.C., U. S. A. F., "physician-scientist who broke existing records for free-balloon flight exceeding 100,000 feet."

Nominations for the Ten Outstanding Young Men of America are solicited annually from the general public and are limited to men between the ages of 21 and 35. Selected by a judging panel of "nationally prominent" persons, the men were chosen "for outstanding contributions to their professions and to the general welfare of the people. The U. S. Jaycees, sponsors of the awards since 1938, distributed more than 15,000 nominations blanks this year.

Symposium on Mechanisms of Hypersensitivity.—An International Symposium on the Mechanisms of Hypersensitivity will be held March 27-29 under the auspices of Henry Ford Hospital, Detroit. About 45 papers are scheduled for presentation including the following by foreign authors:

Heterogeneity of Diphtheria Antitoxins, Dr. Marcel Reynaud, Garches, France.
The Detection of Non-Precipitating Antibodies, Alec H. Sehon, Ph.D., Montreal, Canada.
Approaches to the Problem of Detecting Antibodies, Stephen V. Boyden, Ph.D., Copenhagen, Denmark.
Mechanisms of Hypersensitivity as Revealed by the Actions of Inhibitors, Dr. Heinz O. Schild, London, England.
Non-Specific Chronic Thyroiditis (Hashimoto's Disease), Dr. Deborah Doniach, London, England.
Research on L. E. Cell Formation (Motion Picture), R. Robineaux, Paris, France.
Histamine in Allergic Responses of the Guinea Pig, Dr. Theo Inderbitzen, Zurich, Switzerland.
Antigens Underlying the Phenomenon of Tolerance to Homografting, Leslie Brent, London, England.
Effect of Steroids on Antibody Production, Marvin Darrach, Vancouver, Canada.
The Sensitizing and Adjuvant Effects of Mycobacterial Cells and Fractions, Dr. Robert G. White, London, England.

General discussions will follow the papers. An address will be given by Dr. Robin C. Buerki, executive director, Henry Ford Hospital, at the banquet March 28, at which Dr. Arnold Ashley Miles, London, England, will be the speaker. For information write Henry Ford Hospital, Dr. Joseph H. Shaffer, 2799 West Grand Blvd., Detroit 2.

President's Conference on Occupational Safety.—The President's Conference on Occupational Safety will be held March 25-27 in Washington, D. C.

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Medical participants will include Harry Levinson, Ph.D., director, Division of Industrial Mental Health, The Menninger Foundation, Topeka, Kansas; Dr. William A. Tillmann, department of psychiatry, University of Western Ontario Faculty of Medicine, London, Ontario, Canada; Dr. Flanders Dunbar, editor emeritus, *Psychosomatic Medicine*. Eight workshops are scheduled under the title "What Makes Us Work Safely" to be moderated by Dr. Levinson. A panel discussion, "Radiation—A Controllable Hazard," will be moderated by Admiral Willard A. Kitts III, manager, Atomic Products Study for General Electric. A second panel, "The Doctor and Nurse Contribute to Safety and Health," will be moderated by Dr. Leo J. Wade, medical director, Esso Standard Oil Company, New York City, and will include as participants Dr. Marvin L. Amdur, Buffalo Industrial Medical Center, Buffalo, New York; Edna O'Connor, R.N., Williamson Heater Company, Cincinnati, Ohio; Charlotte R. Burneister, R.N., American Association of Industrial Nurses, Baltimore; Mr. Clark D. Bridges, assistant managing director, Industrial Medical Association, Chicago; and Mr. Howard Schulz, Council of Industrial Health, American Medical Association, Chicago. For information write the U. S. Department of Labor, Washington, D. C.

Medical Writers' Institute.—A Medical Writers' Institute will be held June 12-14 at Rensselaer Polytechnic Institute, Troy, N. Y. The seminar of study and workshop practice will be under the auspices of the Technical Writers' Institute, now entering its sixth session under the direction of Prof. Jay R. Gould. The three-day course will be coordinated by Dr. Joseph F. Montague, president of the New York chapter of the American Medical Writers' Association. Medical writers will serve as visiting lecturers in the fields of medical reports, manuals and instructions, medical advertising and journalism, and medical illustrations. Included will be Dr. Morris Fishbein, president-elect, American Medical Writers' Association; Dr. Benjamin W. Carey, medical director, Lederle Laboratories; Mr. Erwin DiCyan, past-president, Association of Consulting Chemists; Dr. Richard M. Hewitt, Publications Division, Menninger Foundation; Walter Kahoe, Ph.D., medical editor, J. B. Lippincott Company; Dr. Frank H. Netter, medical artist and illustrator; Prof. Carroll A. Nolan, chairman, department of business education, Syracuse University; Mr. Gil Totten, of the William Douglas McAdams Advertising Agency, New York; Dr. Felix Marti-Ibanez, editor, *MD*; and Mr. A. A. Rasch, medical editor, Roswell Park Memorial Institute. The basic instructional phase will be staffed by members of the Technical Writers' Institute, including professors Sterling P. Olmsted, Douglas H. Washburn, Chris Stanford, and Robert A. Sencer. The institute has been designed "to bring expert guidance to those who supervise medical writing, to those newly entering this expanding profession, and to those practicing writers who need an exchange of recent ideas." Inquiries should be addressed to Prof. Jay R. Gould, Medical Writers' Institute, R. P. I., Troy, N. Y.

WARNING—BAD CHECK ARTIST

Attention is called to the illegal activities of one Joseph T. Reddish, formerly of Boston and more recently of Roxbury, Mass., who may be posing as a Doctor of Medicine or as a medical technician in pathological laboratories in hospitals or in private organizations.

Joseph T. Reddish, whose photograph is shown below, is described as aged about 45, height 5 feet 5 inches to 5 feet 7 inches, and weighing about 165

pounds. He has dark brown hair, blue eyes, and a broad face, a ruddy complexion, and a Boston accent. He has claimed to be a laboratory technician, specializing in bacteriology and cytology. He is described as having letters and newspaper clippings claiming that he was associated in the development of an electronic device to screen microscopic slides.

Some months ago he was employed as a technician in a hospital in Newark, N. J. He passed several checks on his representation that he was employed at the hospital. These checks were drawn on the First National Bank of Boston and were returned, marked "No account."

Any person knowing his whereabouts should notify the Director of the Department of Clinical Pathology at the Presbyterian Hospital, Newark, N. J.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: The American medical qualification examination to be given henceforth twice a year for foreign medical graduates. *First Examination.* Medical Schools in the United States, March 25. Final date for filing application was Feb. 10. *Second Examination.* Medical Schools in the United States and Foreign Countries, Sept. 23. Final date for filing application is June 23. Executive Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Illinois.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 17-19. Sec., Dr. D. G. Gill, State Office Building, Montgomery 4.

COLORADO:* *Examination and Reciprocity.* Denver, June 10-11. Exec. Sec., Mrs. Beulah H. Hudgens, 715 Republic Bldg., Denver 2.

CONNECTICUT:* *Examination.* Hartford, March 11-13. Sec., Dr. Creighton Barker, 160 St. Roman St., New Haven. *Homeopathic. Examination.* Derby, March 11. Sec., Dr. Donald A. Davis, Derby.

DELAWARE: *Examination and Reciprocity.* Dover, July 8-10. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

FLORIDA:* *Examination.* Miami, June 29-July 1. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami.

GEORGIA: *Examination and Reciprocity.* Atlanta and Augusta, June. Sec., Mr. C. L. Clifton, 224 State Capitol, Atlanta.

IDAHO: *Examination.* Boise, July 14-16. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

ILLINOIS: *Examination and Reciprocity.* Chicago, April 7-10. Superintendent of Registration, Mr. Fredric B. Selcke, Capitol Bldg., Springfield.

INDIANA: *Examination.* Indianapolis, June 18-20. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

LOUISIANA: *Examination and Reciprocity.* New Orleans, June 3-7. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans.

MAINE: *Examination and Reciprocity.* Portland, Mar. 11-13, Sec., Dr. Adam P. Leighton, Room 514, 152 High St., Portland.

MARYLAND: *Examination.* Baltimore, June 17-20. Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

MASSACHUSETTS: *Examination.* Boston, July 15-18. Sec., Dr. Robert C. Cochrane, Room 37 State House, Boston.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June 9-11. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

MICHIGAN:* *Examination.* Minneapolis, April 15-17. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

MONTANA: *Examination and Reciprocity.* Helena, April 1. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

NEBRASKA:* *Examination.* Omaha, June. Sec., Mr. Husted K. Watson, Room 1069, State Capitol Bldg., Lincoln 9.

NEVADA:* *Examination and Reciprocity.* Reno, March 4. Sec., Dr. G. H. Ross, 112 North Curry St., Carson City.

NEW HAMPSHIRE: *Examination and Reciprocity.* Concord, Mar. 12-14. Sec., Dr. Mary M. Atchison, 107 State House, Concord.

NEW YORK: *Examination.* Albany, Buffalo, New York City and Syracuse, June 24-26. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

NORTH CAROLINA: *Endorsement.* Asheville, May 5. *Examination.* Raleigh, June 16-19. *Endorsement.* Raleigh, June 17. Asst. Sec., Mrs. Louise J. McNeill, Professional Bldg., Raleigh.

OHIO: *Endorsement.* Columbus, April 1; June 19-21. Sec., Dr. H. M. Platter, 21 West Broad St., Columbus 15.

OKLAHOMA:* *Examination.* Oklahoma City, June 3-4. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Examination.* Portland, April 11-12. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

RHODE ISLAND:* *Endorsement.* Providence, March 20. *Examination.* Providence, April 3-4. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH DAKOTA:* *Examination.* Rapid City, August 12-13. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

TENNESSEE:* *Examination.* Memphis, March 19-20, Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.

TEXAS:* *Examination and Reciprocity.* Fort Worth, June 23-25. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Examination.* Salt Lake City, July 9-11. Director, Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

WISCONSIN:* *Endorsement.* Madison, April 25. *Examination.* Milwaukee, July 8-10. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., 1 West Wilson St., Madison.

WYOMING: *Examination and Reciprocity.* Cheyenne, June 2. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

ALASKA:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

GUAM: *Subject to Call.* Act. Sec., Dr. S. F. Provencher, Agana.

PUERTO RICO: *Examination.* San Juan, March 4-7. Sec., Mr. Joaquin Mercado Cruz, Box 9158, Santurce.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* Juneau, Nov. 4. Sec., Dr. R. Harrison Leer, Room 204, Alaska Office Bldg., Juneau.

ARKANSAS: *Examination.* Little Rock, May 5-6. Sec., Mr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.

COLORADO: *Examination and Endorsement.* Denver, May 7-8. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

CONNECTICUT: *Examination and Endorsement.* New Haven, June 14. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 14-15. Deputy Director, Commission on Licensure, Mr. Paul Foley, 1740 Massachusetts Ave., N. W., Washington 6.

IOWA: *Examination.* Des Moines, April 8. Sec., Dr. Elmer W. Hertel, Wartburg College, Waverly.

KANSAS: *Examination.* Kansas City, June 3-4. Sec., Dr. R. E. Stowell, University of Kansas School of Medicine, Kansas City 12.

MINNESOTA: *Examination.* Minneapolis, April 1-2. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis 14.

OKLAHOMA: *Examination.* Oklahoma City, April 4-5. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, March 1. Dr. Earl M. Pallett, Sec., State Board of Higher Education, Eugene.

RHODE ISLAND: *Endorsement.* Providence, April 30. *Examination.* Providence, May 14. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

TEXAS: *Examination.* Austin, April. Sec., Brother Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

WISCONSIN: *Examination.* Madison, March 29, Milwaukee, June 7. Sec., Mr. William H. Barber, 621 Ransom St., Ripon.

*Basic Science Certificate required.

GOVERNMENT SERVICES

VETERANS ADMINISTRATION

The Veteran Population.—The following information appears in the Dec. 31, 1957, Statistical Summary of VA Activities:

Veterans in civil life, end of month—Total	22,710,000
Korean Conflict—Total	5,255,000
And service in World War II	913,000
No service in World War II	4,342,000
World War II—Total	15,315,000
World War I	2,923,000
Other Wars and Regular Establishment b/	130,000
HOSPITAL CARE—ALL WARS	
Average daily patient load—Total	113,028
In VA hospitals	110,048
In non-VA hospitals	2,980
Eligible applicants—admission not scheduled—end of month—Total	20,250
Disabilities adjudicated service-connected	8
Other	20,242
DOMICILIARY CARE—ALL WARS	
Average daily member load	16,821
Eligible applicants—admission not scheduled—end of month	695
OUTPATIENT CARE—ALL WARS	
Visitors for medical care during month—Total	154,007 a/
Outpatient treatment	109,678 a/
Compensation and pension examinations	27,317 a/
Other	17,012 a/
Dental examination cases completed during month	3,286
Dental treatment cases completed during month	3,029
DISABILITY COMPENSATION OR PENSIONS—ALL WARS	
New cases received during month	16,812
New cases adjudicated during month	15,244
New cases pending adjudication, end of month	41,155
Active cases (running awards), end of month	2,817,666
Compensation (service-connected) b/	2,065,630
Pensions (non-service-connected)	752,036
DISABILITY COMPENSATION OR PENSIONS—KOREA	
New cases received during month	5,392
New cases adjudicated during month	4,832
New cases pending adjudication, end of month	14,240
Active cases (running awards), end of month	200,785
Compensation (service-connected)	197,142
Pensions (non-service-connected)	3,643
DEATH COMPENSATION OR PENSIONS—ALL WARS	
New claims received during month	11,135
New claims adjudicated during month	10,441
New claims pending adjudication, end of month	13,287
Active cases (running awards), end of month	867,838
Compensation (service-connected) b/	386,626
Pensions (non-service-connected)	481,212
DEATH COMPENSATION OR PENSIONS—KOREA	
Active cases (running awards), end of month	36,699
Compensation (service-connected)	35,560
Pensions (non-service-connected)	1,139

a/ Preliminary; subject to revision.
b/ Includes special act cases.

Personal.—Dr. Linus A. Zink will succeed Dr. Frank B. Brewer as assistant chief medical director for operations in the VA at Washington, D. C. Dr. Brewer is to retire March 31, 1958, after 41 years of federal service.

AIR FORCE

Consultants Visit Medical Installations.—Dr. Edgar J. Poth, professor of surgery at the University of Texas Medical School, recently visited U. S. Air Force Medical Service installations in Japan, Okinawa, and the Philippine Islands, where he rendered consultant services and conducted lectures.

Dr. Joe C. Rude, chief of radiology, University of Texas Medical School, recently visited Air Force Medical Service installations in Germany, France, England, Morocco, and Libya, where he conducted lectures and teaching sessions. Dr. Rude presented a paper, "Radiographic Contributions to the Diagnosis of Acute Abdominal Conditions," at the U. S. Air Forces in Europe Medical-Surgical Conference in Wiesbaden, Germany.

ARMY

The Bovard Award.—At a ceremony in the Letterman Army General Hospital in San Francisco, Jan. 14, the Evangeline G. Bovard award for 1957 was presented to Capt. Lenora B. Wierick of the Army Nurse Corps. The award was established last year by Col. Robert Skelton, M. C., U. S. Army, retired, in memory of his wife, a former Army nurse. Colonel Skelton set aside a sum of money, the interest on which is to be presented to the nurse demonstrating the highest degree of professional competence in maintaining the superior standards of the Army Nurse Corps.

Captain Wierick served with a front line field hospital in Germany and during the Korean conflict received the Bronze Star for service in the forward areas with a mobile surgical hospital. At Letterman, Captain Wierick has demonstrated outstanding skill in the care of paraplegic and acutely ill patients.

NAVY

Retirements.—Capt. Otto Leo Burton, M. C., commanding officer of the U. S. Naval Medical Research Unit 3, Cairo, Egypt, was retired from active service, Jan. 1, after completing more than 31 years of service.—Capt. Melville M. Driskell, M. C., was placed on the retired list of naval officers on Jan. 1, after completing more than 21 years of military service.

PUBLIC HEALTH SERVICE

Physicians Wanted for Immediate Active Duty.—The Public Health Service is offering immediate active duty assignments to physicians who qualify for appointment to its Commissioned Corps. Physicians who have Selective Service obligations to fulfill can meet them by serving two years active duty in the Commissioned Corps. Public Health Service officers receive the same pay, allowances, and benefits that are received by officers in the armed forces serving on active duty. Officers on active duty are covered by retirement, social security, medical care (both for the officer and his dependents), and a survivor benefits annuity. They are also entitled to sick leave and annual leave with pay.

The majority of assignments given to physicians in the Public Health Service are in clinical medicine, but a limited number are available in research, preventive medicine, and public health. The largest number of positions now available are for medical officers who are completing internship or are in residency training. However, some positions are available for board-eligible or board-certified specialists, e. g., pathologists, radiologists, psychiatrists, internists, surgeons, and pediatricians.

The entrance grade for officers who have completed an approved internship is senior assistant surgeon, the equivalent of captain in the Army. Correspondingly higher grades are given to officers who have had advanced training or additional years of experience following internship. Longevity credit for pay purposes (including service in the armed forces) is also granted.

Inquiries concerning careers in the Public Health Service or two years of active duty to satisfy Selective Service obligations should be directed to the Surgeon General, U. S. Public Health Service (P), Washington 25, D. C.

Graduate Training for Health Workers.—The Public Health Service announced Jan. 28 that it is accepting applications from professional health workers for graduate training in public health for the 1958-1959 academic year. This program was set up by Congress two years ago to help relieve the shortage of trained personnel in public health agencies. Congress voted one million dollars for the first year of the program and two million dollars for the second year. A total of 895 traineeships have been awarded to individuals either directly by the Public Health Service or through grants to public health training institutions. Awards include 67 for physicians; 462, nurses; 94, health educators; 65, sanitarians; 61, sanitary engineers; 29, laboratory workers; 28, dentists; 23, veterinarians; and 17 for nutritionists. In addition to tuition and fees, the traineeships provide stipends covering the living expenses of the trainees and their legal dependents. Applications should be submitted by March 1, 1958.

Personal.—Dr. Stuart M. Sessoms, who has been assistant director of the clinical center at the National Institutes of Health, has been appointed assistant director of the National Cancer Institute, it was announced by Dr. James A. Shannon, director of the National Institutes of Health. Dr. Sessoms succeeds Dr. William S. Baum, who has been transferred to the Public Health Service's Division of Indian Health as assistant area medical officer for hospital and medical care at Phoenix, Ariz.

DEPARTMENT OF STATE

Contribution for Malaria Eradication.—The United States government contributed 7 million dollars on Dec. 5, 1957, to the World Health Organization and the Pan American Sanitary Organization to further their work in assisting governments throughout the world to eradicate malaria. In a ceremony in Washington, D. C., the Secretary of State presented a check of 5 million dollars to WHO Director-General Dr. M. G. Candau, and another check for 2 million dollars to Dr. Fred L. Soper, director, Pan American Sanitary Bureau, Regional Office of WHO for the Americas. In presenting the checks, Secretary of State Dulles said, in part: "it is most fitting that the United States should join with the World Health Organization and the Pan American Sanitary Organization in a unified campaign to eradicate what is possibly the greatest single source of death and sickness in the world today. This is malaria. Last year, malaria attacked some 200,000,000 people. . . . The United States, in accordance with President Eisenhower's recommendation to the Congress, agreed with the goal of malaria eradication set by the 1955 Assembly of the World Health Organization."

What is sought is eradication of the disease from virtually all malarious areas except for Africa south of the Sahara and a few other presently inaccessible places. The international effort will be carried out over a five-year period. For fiscal year 1958, the total expenditure of the United States and 60 other nations, plus the international organizations, is estimated at $107.2 million.

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DEATHS

Acree, Marvin Albin ● Calhoun, Ga.; University of Georgia Medical Department, Augusta, 1912; died Dec. 4, aged 72.

Adams, Justin Orpheus ● Chattanooga, Tenn.; University of Nashville Medical Department, 1895; died Dec. 5, aged 88, of uremia.

Adams, Noah ● Independence, Mo.; Barnes Medical College, St. Louis, 1899; formerly practiced in Kansas City, Mo., where he was associated with the Baptist Hospital; died in the Independence Sanitarium and Hospital Dec. 6, aged 83, of cerebral hemorrhage.

Anderson, William Edward ● Chattanooga, Tenn.; Vanderbilt University School of Medicine, Nashville, 1898; member of the Selective Service Board during World Wars I and II; died Dec. 7, aged 81, of heart disease.

Anthony, Abel Cornelius, Chicago; University of Illinois College of Medicine, Chicago, 1931; on the staff of the Provident Hospital, where he died Dec. 16, aged 57, of pulmonary embolism following a prostatectomy.

Ashley, Charles L. ● Dallas, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1900; an associate member of the American Medical Association; served as county coroner; formerly practiced in Plymouth, where he was registrar of vital statistics and a director and vice-president of the Plymouth National Bank; died Dec. 28, aged 79.

Barenberg, Louis H. ● New York City; born Feb. 20, 1886; Long Island College Hospital, Brooklyn, 1914; specialist certified by the American Board of Pediatrics; member of the New York Academy of Medicine; past-president of the Bronx Pediatric Society; served as clinical professor of pediatrics at the New York Medical College, Flower and Fifth Avenue Hospitals; held an award of merit from the American Medical Association for exhibit in 1942 on "Prevention of Contagion in Pediatric Wards with the Use of Human Serum or Plasma"; associated with the Morrisania City and Jewish Memorial hospitals; died in the Montefiore Hospital Dec. 18, aged 71.

Barnes, Herbert Francis, Worcester, Mass.; Tufts College Medical School, Boston, 1932; associated with the Worcester State Hospital; was killed Dec. 7, aged 57.

● Indicates Member of the American Medical Association.

Barnsback, Roy Smith ● Edwardsville, Ill.; born in Edwardsville Sept. 12, 1876; Vanderbilt University School of Medicine, Nashville, Tenn., 1899; founder and past-president of the Madison County Tuberculosis Association; past-president of the Madison County Medical Society; medical examiner for the draft board during World War II and received a citation from President Roosevelt for his services; a founder and a director of the Edwardsville National Bank and Trust Company; associated with St. Elizabeth Hospital in Granite City, where he died Dec. 9, aged 83, of pulmonary edema and cardiac failure.

Beck, R. Donald, New York City; Columbia University College of Physicians and Surgeons, New York City, 1919; served on the staff of the Goldwater Memorial Hospital; died Dec. 8, aged 64, of coronary disease.

Bennett, Clayton James ● Yuma, Colo.; St. Louis College of Physicians and Surgeons, 1923; member of the American Academy of General Practice; past-president, secretary, and charter member of the Yuma–Washington Counties Medical Society; veteran of World War I; mayor of Yuma eight years and long active in the town council and school board; formerly practiced in La Junta, Colo., and Oak Creek, Colo.; died in the Veterans Administration Hospital, Denver, Dec. 9, aged 66, of bleeding esophageal varices and hepatic failure.

Bernstein, Theodore Isra ● Solvang, Calif.; University of Southern California School of Medicine, Los Angeles, 1938; member of the American Academy of General Practice; decorated by Gen. George Patton for his services to the Third Army Medical Corps in the European invasion during World War II; associated with St. Francis and Cottage hospitals in Santa Barbara; died in the University of California Medical Center in Los Angeles, Dec. 13, aged 47, of leukemia.

Beutel, Georgus Phil, Louisville, Ky.; University of Louisville Medical Department, 1898; an associate member of the American Medical Association; past-president of the Louisville Urological Society; veteran of World War I; served on the Selective Service Board during World War II; died Dec. 18, aged 79, of heart disease.

Bickley, Robert Stanley ● New York City; New York Homeopathic Medical College and Hospital, 1907; formerly clinical professor of surgery at his alma mater; fellow of the American College of Surgeons; associated with Flower and Fifth Avenue

Hospitals and the Medical Arts Center Hospital; died Dec. 26, aged 71, of diabetes mellitus, myocarditis, and arteriosclerosis.

Black, William Davis ● St. Louis; Marion–Sims College of Medicine, St. Louis, 1896; member of the American Academy of Ophthalmology and Otolaryngology; at one time on the faculty of Barnes Medical College; served on the staff of Missouri Baptist Hospital; died Dec. 2, aged 83.

Bloss, Raymond Henry, Bethlehem, Pa.; Medico–Chirurgical College of Philadelphia, 1906; associated with St. Luke's Hospital, where he died Dec. 16, aged 75, of heart disease.

Bogia, Reuben Arnold, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1904; veteran of World War I; served on the city health department; associated with Lankenau, Women's and Children's hospitals; died Dec. 11, aged 76.

Boswell, Henry ● Sanatorium, Miss.; born in Hinton, Ala., March 26, 1884; University of Nashville Medical Department, 1908; became the first full-time field director of the Mississippi State Board of Health and served in that capacity for many years; formerly on the faculty of the University of Mississippi School of Medicine in University; member of the House of Delegates of the American Medical Association from 1922 to 1924, in 1926 and 1928; past-president of the Mississippi State Medical Association; member, past-president, and a member of the executive committee of the National Tuberculosis Association; member and past-president of the Mississippi Tuberculosis Association; member and past-president of the Mississippi State Hospital Association; past-president of the American Sanatorium Association; vice-chairman, board of trustees of mental institutions for Mississippi; chairman of the Mississippi Commission on Hospital Care; member of the Central Medical Society, American Trudeau Society, and the Mississippi Trudeau Society; fellow of the American College of Physicians and American College of Chest Physicians; past-president and honorary life-time president of the Mississippi Golf Association; recipient in 1953 of the Civic Award for service to Mississippi; recently retired as superintendent and medical director of the Mississippi State Sanatorium, where he served since 1917, and where he died Dec. 16, aged 73, of chronic pulmonary emphysema and bronchogenic carcinoma with metastases.

Brabrook, Caroline Alexander, Whittier, Calif.; Northwestern University Woman's Medical School, Chicago, 1893; died Nov. 17, aged 87.

Brueckner, Harold Hugo ● Canton, Ohio; University of Michigan Medical School, Ann Arbor, 1932; member of the American College of Chest Physicians and the American Trudeau Society; at one time on the faculty of the University of Louisville (Ky.) School of Medicine; served as superintendent of the Molly Stark Hospital; formerly superintendent of the District Tuberculosis Hospital in Lima, Ohio; died in Ann Arbor, Mich., Dec. 8, aged 50, of uremia and bilateral polycystic kidney disease.

Buford, Coleman Graves ● West Palm Beach, Fla.; Northwestern University Medical School, Chicago, 1894; a founder of the American College of Surgeons; past-president of the Northside Branch of the Chicago Medical Society; formerly on the faculty of his alma mater; at one time practiced in Chicago and Elizabeth, Ill.; served on the staffs of St. Luke's, Chicago Polyclinic, Henrotin, Children's Memorial, and Mercy hospitals in Chicago; died Dec. 23, aged 85, of angina pectoris.

Buresch–Henke, Hildegard Ida Louise Charlotte ● Montgomery, Ala.; Schlesische–Friedrich–Wilhelms–Universität Medizinische Fakultät, Breslau, Prussia, Germany, 1936; on the staff of St. Jude's Catholic Hospital; died Dec. 15, aged 60, of endocarditis.

Burkhardt, William Lincoln ● San Antonio, Texas; Northwestern University Medical School, Chicago, 1947; formerly on the faculty of his alma mater; served as chief of professional services at the U. S. A. F. Hospital in Randolph Air Force Base, Randolph Field; died Dec. 1, aged 39.

Burtnick, Lester Leon ● Washington, D. C.; University of Maryland School of Medicine, and College of Physicians and Surgeons, Baltimore, 1937; clinical assistant professor of psychiatry at Georgetown University School of Medicine; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; veteran of World War II; died in the George Washington University Hospital Dec. 16, aged 47, of lymphosarcoma.

Byron, Charles Stanford ● Brooklyn; Cornell University Medical College, New York City, 1923; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the Endocrine Society; associated with Brooklyn Jewish, Adelphi, and Queens General hospitals; died Dec. 26, aged 59, of fibrosarcoma of the left leg with pulmonary and intraperitoneal metastasis.

Canter, Noland Mackenzie ● Harrisonburg, Va.; born in Fredericksburg, July 22, 1890; Johns Hopkins University School of Medicine, Baltimore, 1913; veteran of World War I; captain in the medical corps of the U. S. Army from 1917 to 1920; formerly radiologist at the Walter Reed Hospital in Washington, D. C., assistant radiologist at St.

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Joseph's Hospital and assistant dispensary physician at Johns Hopkins Hospital in Baltimore; member of the Radiological Society of North America; in 1955 received the doctor of science degree from Randolph-Macon College, Ashland; first radiologist, a position held for 27 years, Rockingham Memorial Hospital, where he died Dec. 9, aged 67, of coronary thrombosis.

Carroll, Chester David, New York City; Tufts College Medical School, Boston, 1927; member of the Medical Society of the State of New York; veteran of World War I; died in the Brooklyn Hospital Dec. 6, aged 64, of arteriosclerosis, and myocardial infarction.

Chaffee, Spencer Norman • Solomon, Kan.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; on the staff of the Dickinson County Hospital, Abilene; died Dec. 11, aged 89, of cerebral arteriosclerosis.

Chapman, Dan Williams • Selma, Ala.; University of Cincinnati College of Medicine, 1946; formerly a resident at the Ochsner Foundation Hospital in New Orleans; veteran of World War II; died in the Selma Baptist Hospital Dec. 11, aged 35, of burns received when his bed was destroyed by fire.

Chrisman, John Hall, Owenton, Ky.; Kentucky School of Medicine, Louisville, 1892; veteran of World War I; served on the staff of the Owen County War Memorial Hospital; died Dec. 6, aged 88, of a heart attack.

Colcord, Albert Jackson • Port Allegany, Pa.; University of Buffalo School of Medicine, 1911; died Oct. 27, aged 69, of cancer of the bladder.

Cole, Harold Paul • Thurman, Iowa; Northwestern University Medical School, Chicago, 1911; served on the school board; president of the Thurman State Bank; died in the Jennie Edmundson Hospital, Council Bluffs, Dec. 9, aged 69, of coronary occlusion.

Collins, Dean Albert, Princeton, N. J.; born in Caledonia, Minn., Oct. 14, 1904; University of Minnesota Medical School, Minneapolis, 1934; instructor in physiology at his alma mater from 1930 to 1937; research professor of pharmacology at Temple University School of Medicine, Philadelphia, where in 1937 he became assistant professor of physiology, which post he held until 1941, when he was promoted to associate professor, from 1945 to 1948 served as professor of physiology and from 1948 to 1956 professor and head of the department of pharmacology; from 1943 to 1945 was associate professor of physiology at the University of Illinois College of Medicine in Chicago; member of the American Physiological Society, the Society of Experimental Biology and Medicine, American Association for the Advancement of Science, and American Heart Association; died Dec. 3, aged 53, of myocardial infarction.

Crawford, Rena, New Orleans; Johns Hopkins University School of Medicine, Baltimore, 1915; served on the faculty of the Louisiana State University School of Medicine; member of the American Academy of Pediatrics; for many years associated with Southern Baptist Hospital, where she died Dec. 15, aged 79.

Currie, Ray Edward, Oakland, Calif.; Northwestern University Medical School, Chicago, 1931; for many years served in the regular Army; veteran of World War II; associated with Herrick Memorial Hospital in Berkeley; died in Spokane, Wash., Nov. 16, aged 52, of carcinoma.

Kennedy, Robert Bryson • Detroit; born in Valley City, N. D., May 14, 1895; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1918; specialist certified by the American Board of Obstetrics and Gynecology; past-president of the Michigan Society of Obstetricians and Gynecologists; member of the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; formerly on the faculty of Wayne University College of Medicine; served as chief of the department of obstetrics at Woman's Hospital and St. Joseph's Mercy Hospital; died in West Palm Beach, Fla., Dec. 17, aged 62, of myocardial infarction and arteriosclerotic heart disease.

Kittrell, John Moore • Jena, La.; Tulane University School of Medicine, New Orleans, 1920; served as vice-president of the Rapides Parish Medical Society; veteran of World War I; formerly director of the Jones County (Miss.) Health Department; chief of Jena Hospital; on the staffs of St. Frances Cabrini Hospital and Baptist Hospital in Alexandria; died in Laurel, Miss., Dec. 26, aged 61, of acute pulmonary edema.

Kriz, Rudolph Edmund, Lynch, Neb.; University of Nebraska College of Medicine, Omaha, 1917; served as president of the Holt Northwest County Medical Society; during World War II appointed medical consultant for the Selective Service System and for this service received presidential recognition; for many years on the staff of the Sacred Heart Hospital; vice-president of the Lynch and Bristow banks; died in the Bishop Clarkson Memorial Hospital, Omaha, Dec. 13, aged 65, of uremia.

LoCricchio, John • Youngstown, Ohio; University of Michigan Medical School, Ann Arbor, 1931; specialist certified by the American Board of Pathology; fellow of the American Society of Clinical Pathologists; formerly on the staff of Lima Memorial and St. Rita's hospitals in Lima, Christian H. Buhl Hospital in Sharon, Pa., and St. Vincent's

Hospital in Bridgeport, Conn.; chief pathologist and director of laboratories, St. Elizabeth Hospital, where he died Dec. 28, aged 53, of myocardial infarction.

Lowe, Charles Reuben ● Boise, Idaho; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1911; served as superintendent of the State Hospital South in Blackfoot and the Nampa State School and Colony in Nampa; veteran of World War I; died Dec. 16, aged 78.

Lowry, David O. ● Cooper, Texas; Memphis (Tenn.) Hospital Medical College, 1901; member of the American Academy of General Practice; veteran of the Spanish–American War; died Dec. 16, aged 82, of a heart attack.

Makowski, Dean ● New York City; Jefferson Medical College of Philadelphia, 1930; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the International College of Surgeons; associate clinical professor of urology at the New York University College of Medicine and the New York University Post-Graduate Medical School; associated with New York University–Bellevue Medical Center and St. Luke's Hospital; died Dec. 22, aged 54, of coronary occlusion.

McClelland, Joseph Edgar ● Cleveland; Western Reserve University School of Medicine, Cleveland, 1912; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; formerly on the faculty of his alma mater; served in France during World War I; associated with Babies and Childrens Hospital; died in the Lakeside Hospital Dec. 17, aged 70, of cerebral embolism.

McIntyre, Howard Dixon ● Cincinnati; born in Boulder, Mont., Nov. 10, 1891; University of Cincinnati College of Medicine, 1920; clinical professor of neurology at his alma mater; specialist certified by the American Board of Psychiatry and Neurology; member of the American Academy of Neurology, American Psychiatric Association, and the Central Neuropsychiatric Association; acted as medicolegal psychiatric consultant to the courts of Hamilton County; consultant to many railroads, including Pennsylvania, Southern, Baltimore and Ohio, and the Louisville and Nashville; associated with Cincinnati General, Children's, Dunham, and St. Francis hospitals; member and past-president of the staff of the Good Samaritan Hospital, where he died Dec. 22, aged 66.

McKinstry, Guy Hale ● Washington, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1910; past-president of the Washington County Medical Society; a member of the Blue Shield of Pennsylvania from its inception and was its executive director for ten years; past-president of the Washington Rotary Club; formerly practiced in Pittsburgh, where he was associated with St. Margaret's Hospital; director and president of Hillsview Clinic; died Dec. 22, aged 73.

McMurray, Frederick Arnold ● Vashon, Wash.; Rush Medical College, Chicago, 1920; died Dec. 16, aged 65, of cancer of the kidney.

Mountford, Arthur Harold, Tuscaloosa, Ala.; University of Vermont College of Medicine, Burlington, 1912; specialist certified by the American Board of Psychiatry and Neurology; service member of the American Medical Association; served as manager of the Veterans Administration Hospital; retired from the Veterans Administration March 31, 1956; died Dec. 18, aged 71, of cerebral vascular accident and arteriosclerosis.

Rucker, Henry Cowles ● Chula, Va.; Columbian University Medical Department, Washington, D. C., 1902; past-president of the Amelia County Medical Society; died in St. Luke's Hospital, Richmond, Dec. 22, aged 79, of carcinoma of the stomach.

Sadler, William Loyd, Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1913; assistant clinical professor of surgery at his alma mater; died Dec. 10, aged 73.

Schaeffer, Joseph Randall ● Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1936; on the staffs of the Germantown Hospital and the Nazareth Hospital, where he died Dec. 27, aged 47, of hypertension and arteriosclerotic cardiovascular disease.

Schilling, Falko Wilhelm, Manchester, N. H.; Friedrich–Wilhelms–Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1911; member of the American Academy of General Practice and past-president of the New Hampshire Chapter; a staff member of the Notre Dame Hospital, where he died Dec. 7, aged 72, of acute leukemia.

Schorr, Robert Lee ● Detroit; Detroit College of Medicine, 1893; served on the staff of the Harper Hospital; died Dec. 11, aged 84, of coronary occlusion.

Siragusa, Matteo, Brooklyn; Regia Università degli Studi di Palermo. Facoltà di Medicina e Chirurgia, Italy, 1905; died in San Remo, Italy, Dec. 30, aged 80.

Slack, Harry Richmond Jr. ● Baltimore; born in La Grange, Ga., Nov. 29, 1888; Johns Hopkins University School of Medicine, Baltimore, 1912; assistant professor emeritus of laryngology and otology at his alma mater; visiting professor of otolaryngology at the Peking Union Medical College in Peking, China, 1922-1923; fellow of the American College of Surgeons; veteran of World War I; associated

with the Hospital for Women, Presbyterian Eye, Ear and Throat Hospital, Church Home and Infirmary, Bon Secours Hospital, and Union Memorial Hospital; died Dec. 12, aged 69, of myocardial degeneration and arteriosclerosis.

Smith, Linton S. • Atlanta, Ga.; Atlanta College of Physicians and Surgeons, 1902; served on the staffs of the Georgia Baptist and Crawford W. Long Memorial hospitals; died Dec. 10, aged 76, of coronary thrombosis.

Taylor, Charles Irwin • Pomeroy, Iowa; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; associated with St. Joseph Mercy Hospital and Lutheran Hospital; died Nov. 15, aged 86, of cerebral hemorrhage.

Taylor, John Goodwin • Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1919; certified by the National Board of Medical Examiners; served on the staff of the Methodist Episcopal Hospital, where he died Dec. 23, aged 66.

Terrill, Frank Irving • Deer Lodge, Mont.; University of Michigan Medical School, Ann Arbor, 1925; first president of the Montana Trudeau Society; member of the American College of Chest Physicians; fellow of the American College of Surgeons; medical superintendent of the Montana State Tuberculosis Sanitarium; died Dec. 21, aged 56, of myocardial failure.

Thomas, Belle, St. Petersburg, Fla.; Cornell University Medical College, New York City, 1907; member of the Medical Society of the State of New York; an associate member of the American Medical Association; died in Hendersonville, N. C., Nov. 9, aged 87.

Tuby, Martin H., Brooklyn; New York Homeopathic Medical College and Flower Hospital, New York City, 1929; served on the Selective Service Board during World War II; member of the Medical Society of the State of New York and the American Association of Railway Surgeons; associate surgeon at the Swedish Hospital, where he died Dec. 26, aged 52, of a cerebral accident.

Tumarkin, Joseph S., Miami Beach, Fla.; University of Moscow Faculty of Medicine, Russia, 1924; died Nov. 15, aged 60.

Verbrick, Willard Conrad, Little Chute, Wis.; Marquette University School of Medicine, Milwaukee, 1928; an associate member of the American Medical Association; on the staff of the Central State Hospital in Waupun; died Nov. 19, aged 56, of coronary occlusion.

Wagner, James Holliday, Selma, Calif.; Vanderbilt University School of Medicine, Nashville, Tenn., 1896; served as county health officer; formerly on the staffs of Burnett Sanitarium in Fresno and the Fowler Municipal Hospital, where he died Dec. 22, aged 84, of cerebral thrombosis.

Walo, Theresa J., Miami, Fla.; Homeopathic Medical College of Missouri, St. Louis, 1907; died Dec. 7, aged 88.

Watson, Lois Holmes Brock • San Francisco; University of California School of Medicine, San Francisco, 1928; specialist certified by the American Board of Obstetrics and Gynecology; associate clinical professor of obstetrics and gynecology at her alma mater; past-chairman of the medical staff, Children's Hospital; died in the Notre Dame Hospital Nov. 26, aged 56, of carcinoma of the ovary.

Wayland, Raymond Theodore • San Jose, Calif.; Jefferson Medical College of Philadelphia, 1913; fellow of the American College of Surgeons; past-president of the Santa Clara County Medical Society; a founder and for three years president of the staff at San Jose Hospital, where he died Dec. 16, aged 67.

Weissmiller, Lester Lee • Rutland Heights, Mass.; University of Wisconsin Medical School, Madison, 1930; member of the Louisiana State Medical Society; fellow of the American College of Hospital Administrators and the American Hospital Association; veteran of World War II; at one time medical director of the Ochsner Foundation Hospital in New Orleans; manager of the Veterans Administration Hospital, where he died Dec. 7, aged 54, of coronary thrombosis with acute anterior myocardial infarction.

Williams, James Ernest, Doniphan, Mo.; National University of Arts and Sciences Medical Department, St. Louis, 1913; died in the Doctors Hospital, Poplar Bluff, Nov. 16, aged 77, of arteriosclerotic cardiovascular disease.

Windmueller, Charles R. A., Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; died Dec. 24, aged 79, of cirrhosis of the liver.

Yates, Marion Twitty, Captain, U. S. Navy, Opa Locka, Fla.; Medical College of South Carolina, Charleston, 1935; service member of the American Medical Association; entered the U. S. Navy in 1937; a medical officer 21 years, having served on three ships, in seven base hospitals, and in Hawaii; awarded the Purple Heart during World War II; received many distinguished medals; died in the U. S. Marine Corps Air Station in Miami Dec. 14, aged 48, of coronary thrombosis.

York, Alexander Arthur • High Point, N. C.; Medical Department of Grant University, Chattanooga, Tenn., 1907; died in Durham Dec. 10, aged 80.

FOREIGN LETTERS

CANADA

What Does the General Practitioner Do?—Much light is cast on the nature of the work of Ontario general practitioners by a study recently made by the Statistical and Research Department of Physicians Services Inc. This organization studied 140,000 account cards submitted by members in March, 1957, and found that general practitioners still have most of the office visits, home calls, and night calls, the figure for office visits being 78% and for home calls 85% of the total. They gave 64% of the general anesthetics, and were responsible for 56% of all electrocardiogram interpretations and 40% of all roentgenological interpretations. They also do about 50% of the laboratory procedures and 33% of the endoscopies. They were found to do almost 50% of the appendectomies, no less than 40% of gallbladder and hernia operations, and about 25% of the operations on the stomach, duodenum, and colon. They were also responsible for 50% of the hemorrhoidectomies and tonsillectomies, and 25% of varicose vein ligations. They performed nearly 33% of standard obstetric and gynecological procedures, including cesarean section, dilatation and curettage, and hysterectomy and ovariotomy but did little otolaryngological, neurosurgical, ophthalmological, radiotherapeutic, and formal psychotherapeutic work. About 14% of the plastic surgery and urology was in their hands, and they managed 81% of the dislocations and 71% of the fractures. Other activities mainly within the sphere of the general practitioner were well-baby care (73%), obstetrics (72%), minor surgery (70%), and preventive injections (78%).

Systolic Murmurs in Mitral Stenosis.—Interpretation of the significance of an apical systolic murmur has become of great practical importance with the advent of mitral surgery. Gialloreto and co-workers (*Canad. M. A. J.* 77:1085, 1957) therefore analyzed the first 150 patients operated on in their hospital for mitral stenosis, with particular reference to the murmurs present. Of these, all were shown to have a mitral stenosis at operation; 73 had had a mitral systolic murmur previously. Nevertheless, in only 16 of these patients was mitral insufficiency verified at operation when a regurgitant jet was felt with the finger, over the mitral valve. Unfortunately the regurgitant jet was also felt in three patients without a systolic murmur. In 27 others the murmur was interpreted as a sign of tricuspid insufficiency, while in another 30 no explanation could be given of the murmur, which was probably associated in some unknown way with the mitral lesion. Hence it would seem that a mitral systolic murmur does not contraindicate operation provided it does not represent a predominant mitral regurgitation. This possibility should be eliminated by careful study of symptoms and of the murmur, together with aid from fluoroscopy and routine electrocardiography. If the latter reveal signs of left ventricular hypertrophy, operation is contraindicated. Cardiac catheterization is reserved for exceptional cases. Techniques for exploring the left auricle, with recording of pressures, angiocardiography, electrokymography, and calculation of mitral surface seem superfluous in most patients.

Canadian Conference on Nursing.—Because an increasing number of problems cannot be solved by nursing leaders alone, a conference was called in Ottawa in November with representation from health authorities, nurses, physicians, hospitals, governments, voluntary agencies, and others. After plenary sessions and meetings of study groups, the conference recommended that (1) nurse training be an educational process, preferably through a school planning and controlling the complete education, (2) the budget of the nursing school be separated from any budget of the hospital in general, (3) research projects be undertaken by interested agencies to determine the needs of the public for nursing services, the types of personnel now meeting those needs, the possibility of reassignment of tasks to existing and new groups of nursing personnel, and the best and most economical ways of preparing nursing personnel, (4) the Canadian Nurses' Association investigate methods of expanding recruitment, selection, and training of nurses for advanced studies, (5) all planning for nursing education include planning for preparation of the nursing assistant, (6) liaison be improved with organized medical and hospital groups and with government and other agencies, (7) pressure to learn scientific techniques not be allowed to submerge the art of nursing, and that the importance of the human relationship be constantly emphasized, and (8) attention be given to provision of nursing care in the home in the expanding hospital care program.

Costs of Hospital Care Insurance.—Insurance agencies have long used the waiting period as a device to cut down costs of insurance and to deter insured

The items in these letters are contributed by regular correspondents in the various foreign countries.

persons from excessive use of coverage. In the hospital insurance field, the application of a waiting period of three days, for example, means that on each admission the insured finances himself the first three days of his hospital stay and the agency then takes over the bill. Mindful of the imminence of a hospital insurance plan for Ontario and other provinces, Sellers, (*Canad. M. A. J.* 77:1132, 1957) made some calculations of the effect of imposing an absolute waiting period on the cost of a plan universally applied in Ontario. Basing his calculations on statistics for Ontario public general hospitals in 1951, he showed that a waiting period of three days for hospital benefits would eliminate from benefit about 30% of all patients hospitalized, and about 25% of all hospital days. Hence application of such a waiting period would substantially reduce the cost of a hospital plan and therefore of the premiums, while the direct cost to subscribers would be small. The alternative of restricting benefits to patients with a stay of more than three (i. e., paying for the first three days out of the insurance fund if the patient stays more than three days) is not nearly so satisfactory, for only 5% of hospital days would be eliminated by this method.

Renal Failure.—Palmer and co-workers (*Canad. M. A. J.* 77:11, 1957) summarized their methods of management of renal failure, stressing the importance of dialysis in certain cases. In a second paper (*Canad. M. A. J.* 77:1078) they discussed the clinical features of their series of 54 patients treated for acute renal failure over a period of 10 years. They point out that about 67% of the patients had ischemic nephrosis, mostly following such obstetric complications as abortion and eclampsia or major operation with shock or severe crushing injury. In these patients shock causing severe renal ischemia was a more potent factor in failure than hemolysis alone. Only two cases could be ascribed to transfusion reactions. The other 33% had nephrotoxic nephrosis, mainly due to carbon tetrachloride poisoning, acute alcoholism, or mercuric chloride poisoning. There was one patient with acute glomerulonephritis. The most notable clinical feature was severe oliguria, persisting for a week or longer, and the most characteristic feature was an azotemia of progressive severity with early and persistent gastrointestinal manifestations and late cerebral disturbances. Overhydration was probably present in all patients though only manifest clinically in 50% as pulmonary or peripheral edema, and it likely contributed to symptoms in all patients. It was entirely due to errors of management. Anemia was most marked in the ischemic group. The only severe electrolyte disturbance was hyperkalemia, which caused death in one patient and correlated poorly with electrocardiographic changes. With the onset of diuresis, usually in the second week, recovery was rapid but azotemia became worse for a few days until excretory function became effective. The mortality rate of 50% was worse in the ischemic group than in the nephrotoxic group.

DENMARK

X-ray Treatment of Tonsillitis.—Hansen and Secher (*Nordisk medicin*, Nov. 28, 1957) sent a questionnaire to the 142 patients given x-ray treatment for their tonsillitis. Of the 119 who replied, 25 were men, 47 were women, and 47 were children. Most of the children were given this treatment for hypertrophy of the tonsils and most of the adults for chronic tonsillitis. Some had been febrile, with full-blown angina faucium, and had preferred the x-rays to tonsillectomy. Complete recovery after treatment was claimed in 37%, marked improvement in 38%, slight improvement in 5%, and no improvement in 20%. An average of 15 to 20 days of sickness yearly from this cause occurred before the institution of this treatment and after it only 5 days of sickness occurred yearly. Tonsillectomy was subsequently performed in 19%. Transient discomfort from the treatment, such as dryness of the throat, was experienced in 20%. It was concluded that x-ray treatment may be indicated for tonsillitis when (1) the symptoms are not severe enough clearly to indicate tonsillectomy, (2) operative treatment is contraindicated, (3) the patient refuses operation, or (4) an epidemic of poliomyelitis is present in the community.

Medicolegal Problems.—The Retslaegeraad is an official body whose task it is to deal with disciplinary and other cases in which the medical profession and certain ancillary services are involved. The annual report for 1954 of this body, according to *Ugeskrift for læger*, Dec. 12, 1957, covers a wide range of subjects, from paternity cases and criminal abortions to lapses from sobriety and the practice of medicine by quacks, and deals in detail with 41 of the 3,872 cases dealt with in this year. Problems concerned with castration or sterilization arose in 483 cases including that of the man given permission to submit to sterilization on the plea that his wife was frail in consequence of infantile paralysis contracted in childhood. There were 1,041 cases hinging on alcohol. In one of them the Retslaegeraad was asked to explain how two persons consuming the same quantity of alcohol could have different concentrations of alcohol in their blood (0.07 and 0.16% respectively). In the answer it was suggested that these data tend to stultify the evidence provided by blood tests for the alcohol level. One of the cases of quackery dealt with was that of a boy whose poliomyelitis was treated in an acute, febrile stage by a quack. The boy's right arm became paralyzed. On the assumption that this paralysis had been aggravated by inadequate rest and a faulty

posture of the arm, and also on the assumption that the boy was infectious at the time, the quack was given 60 days in prison. In 43 cases the Retslaegeraad had to deal with mishaps caused by drugs given injudiciously. In one such case a nurse on duty in a home for old folk had been confronted by one of its inmates the worse for liquor. To soothe him she gave him chloral with morphine from which he died a few hours later. Evidently she had been unaware of the observation that a previous dose of alcohol may render fatal a dose of morphine which would otherwise have been innocuous. She could hardly have been expected to know this and was accordingly exonerated.

Allergy to Coffee.—Dr. E. Bruun (*Nordisk medicin*, December, 1957) reported a series of six patients with allergy to coffee due to occupational exposure. Their ages ranged from 15 to 34 years, and their exposure to coffee had lasted only a short time. The most common complaint was vasomotor rhinitis, but in some asthma and angioneurotic edema occurred. None of the patients suffered from eczema. Their symptoms were coterminous with exposure to coffee, ceasing when they were on holiday. Intracutaneous injections of coffee extracts gave positive reactions even when the dosage was very minute. The cutaneous allergy was equally marked whether the extract was from the bean or from ground coffee but there was no reaction from coffee which had been boiled for three minutes. This may explain why the patients could drink coffee with impunity, the allergen at fault having evidently been destroyed by boiling. Four of the patients also showed cutaneous allergy to hazel nuts which may therefore possibly contain a closely related allergen. The law provides compensation for the victims of eczema and asthma provoked by allergy to flour, and Bruun suggested that similar compensation be extended to the victims of allergy to coffee.

Standardization of Sutures.—In 1954 the Danish Surgical Society appointed a committee to deal with the standardization of suture materials. In *Ugeskrift for læger*, Jan. 9, Dr. Madsen reported that this committee has revolutionized one supply problem of operation rooms where the nurse in charge used to have to memorize the requirements of different surgeons. Henceforth surgeons need not worry about the conflicting claims of different preparations, but can rely on the guarantee of the standardized material available for their use. The cost of suture material has been reduced by the elimination of different brands which were formerly kept in stock even though the demand for them may have been small.

The Prognosis in Epilepsy.—Kiörboe and co-workers (*Ugeskrift for læger*, Jan. 2, 1958) reported a follow-up study of 130 epileptics whose epilepsy had begun after the age of 17 years. They were among the 156 epileptics who, four to seven years earlier, had been admitted to hospital on account of this disease. During this interval 13 had died, but in only one case had death been traceable to the epilepsy (drowning during a seizure). An electroencephalogram was made both at the first examination and at the follow-up. The first tracings by themselves proved of little value to the prognosis, whereas when repeated they proved helpful. In 85% of the patients, the course of the disease was much the same in the first year of observation as in the following years. About 45% were free from seizures for at least four years. The patients with automatic epilepsy had a worse prognosis than those with other types. It was concluded that, as a rule, the epileptic who has had no seizure for two years may be granted a license to drive a car, the risk of his having a seizure while driving being presumably less than the risk that the elderly driver will have a coronary thrombosis or cerebral hemorrhage. Of the 12,000 traffic accidents dealt with in a hospital in 1954, only 18 were traced to an epileptic seizure; but balanced against these figures must be those showing that about 5% of the 680 epileptics driving cars between 1953 and 1955 were held responsible for traffic accidents. Because of the necessity for workers in many industries, even farming, to be free to drive a car in order to make a living, the authors plead for a fair deal for the epileptic.

INDIA

Hypothermic Cardiac Arrest.—P. K. Sen and co-workers (*Indian Journal of Medical Sciences*, vol. 11, December, 1957) stated that open cardiac surgery under hypothermia is limited primarily by the short period for which the heart can be excluded from the circulation without causing permanent damage to the brain. The chilled heart is also particularly susceptible to ventricular fibrillation during such procedures. Greater technical accuracy is possible, however, when the heart rate is slowed by hypothermia. The safe limit for inflow occlusion should also then be greatly increased. A preliminary series of experiments were therefore performed on dogs, with use of surface cooling to produce hypothermia; 18 healthy adult dogs were anesthetized with thiopental sodium and subjected to severe hypothermia. Hyperventilation was carried out by means of a positive-pressure pump connected to an endotracheal cuff tube. Cooling was continued until arrest or near-arrest developed. The lowest rectal temperatures recorded were between 9 and 15 C. Total cardiac arrest occurred in seven, while in the rest the heart rate fell to six per minute or lower. The period of arrest or near-arrest varied between 15 and 20 minutes. Rewarming was

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done by immersion in warm water at 45 C. Hyperventilation was continued except during the period of total arrest. Fourteen dogs survived the experiment on being rewarmed. Of the seven with complete cardiac arrest, four survived with resumption of normal cardiac activity on rewarming. No thoracotomy or cardiotomy was performed. During cooling the fall in body temperature was uniformly rapid down to 20 C which was reached in an hour. Further reduction in temperature became progressively slower and sometimes took four to seven hours.

Electrocardiographic tracings showed a progressive slowing in conduction of the impulse through the heart, more so during repolarization than depolarization. Major conduction blocks were not frequent nor were ectopic beats. Ventricular fibrillation was not observed in this series, but ventricular or nodal rhythms at temperatures below 18 C were common. Auricular standstill often developed at this stage. The absence of ventricular fibrillation may be due to continuous hyperventilation and the absence of surgical or mechanical insult to the heart or great vessels. Certain general changes were noticed after recovery as a sequel to the deep hypothermia. There was a general loss of hair and the hair took weeks to reappear, that on the shaven parts being affected most. The animals lost 3 to 7 kg. in the first two or three postoperative weeks. This may have been due to the severe stress of the hypothermic process and the consequent negative nitrogen balance.

Hepatic Cirrhosis.—M. N. Bhattacharya (*Antiseptic*, vol. 55, January, 1958) studied 200 cases of cirrhosis of the liver in the Assam Medical College Hospitals. The diagnosis was based mainly on clinical features and liver function tests. Patients with clinical manifestations of hepatic insufficiency, with an enlarged liver but without a palpable spleen, and those with enlarged spleens and ascites, but without any complaints pointing to hepatic insufficiency, were subjected to liver function tests and if these showed a disturbed liver function, a diagnosis of cirrhosis was made. A patient with clinical features of hepatic insufficiency, an enlarged spleen, ascites, and with or without an enlarged irregular liver was given a diagnosis of cirrhosis. Of these cases, 73% occurred in the age group of 20 to 49 years, the maximum incidence being in the fourth decade; 80.5% were men and 19.5% were women. About 90% came from the low income groups; 7% gave a history of infective hepatitis; and 21% were alcoholic. Swelling of the abdomen and edema of the legs were the commonest complaints for which patients sought medical advice. The blood pressures were within the normal range. Estimations of blood proteins gave low values for total blood protein and albumin while globulin was increased and the albumin-globulin ratio was decreased. Leukocyte counts were within normal range. About 93.5% had hemoglobin values below 70%. Stools from 56% of the patients contained parasites. Bronchitis complicated 18.5%; pyelonephritis 15%; and tuberculosis 1.5% of the cases.

Thus, in this series, cirrhosis of the liver was seen to occur in an earlier age group than in the western countries. Nearly all cirrhotic patients suffered from protein deficiency and, except for infective hepatitis and alcoholism which together accounted for 28% of the patients, nutritional deficiency, primary or secondary to tropical diseases, was the chief factor in the production of the cirrhosis. Most of the patients either missed the early symptoms of hepatic insufficiency such as nausea, anorexia, and flatulence or did not have them and came for treatment at a later stage when ascites or edema had already appeared. The high incidence in the low-income group is related to deficiency of protein in the diet, while secondary nutritional deficiency resulting from tropical diseases, loose stools, and intestinal parasites was also commonly seen in this series.

Trachoma.—Speaking at the National Seminar on Communicable Eye Diseases, Dr. C. G. Pandit, Director of the Indian Council of Medical Research, said that trachoma is the greatest single cause of blindness in India. He stressed the need for a mass control program. Dr. M. Radovanovic, World Health Organization senior adviser to the Trachoma Pilot Project, said that an ophthalmologist when presented with a patient with trachoma must look not merely at the eye but must also seek the environmental, cultural, and personal habits that predisposed the patient to trachoma or any other eye infection.

Association of Medical Women.—Inaugurating the Golden Jubilee Session of the Association of Medical Women in December in Bombay, the Minister for Health stated that the government is considering the formation of a Central Health Cadre and hoped that women with necessary training and experience would be available for inclusion in this central service when it came into existence. He suggested that the younger members of the association should venture into various fields of medicine and assured the organization of the government's fullest support. He said that medical women can fill a special need in such fields as school health, family planning, health education, and tuberculosis work among women and children.

Maternal and Child Health.—According to the report of the World Health Organization regional director for Southeast Asia, it has come to be realized that in order to serve a community best in the field of maternal and child health a community health program is needed in which the mother and child are given special attention. Where malnutri-

tion and infectious diseases are still widespread, it is not practicable to attempt to meet the needs through services in which curative and preventive care are separated. The present position in child care in all countries of the region is that there is a division between curative services which are given by physicians in hospitals or outpatient clinics and are mostly limited to towns, and preventive services which are mainly the domain of auxiliary personnel occasionally supervised by medical staff. In the future, in order to secure adequate and effective services for children, it will be essential to improve the teaching of pediatrics in medical schools. Great progress has been made in the teaching of pediatrics in several medical colleges in India specifically in connection with WHO-UNICEF-assisted maternal and child health projects. In Nagpur an independent department of pediatrics was created and teaching was extended to three months. A child welfare clinic was set up on the medical college grounds and a separate clinic for spastic children, the first in the region, was also established. In Hyderabad, two child health centers were established in order to demonstrate to the students the unity of the preventive and curative aspects of child care. In Lucknow the two child welfare centers already established were adapted for use as a supplement to the academic courses in preventive pediatrics. On the suggestion of WHO personnel, the teaching of pediatrics in the first clinical year will consist of the growth, development, and supervision of the normal child. Only after that will the students be taught the pathology of childhood.

Peptic Ulcer.—Bamji and Mudur (*Current Medical Practice*, vol. 1, December, 1957) used oxyphenonium bromide, a synthetic anticholinergic quaternary ammonium compound, in the treatment of 39 patients with chronic peptic ulcer; 38 of these were men. All patients had duodenal ulcer except one who showed no radiologic evidence of ulcer but had a history typical of peptic ulcer and hyperacidity. Most of the patients were between 20 and 39, but three were between 60 and 65. The presenting symptom was pain in the abdomen, mostly in the epigastrium, though three patients had pain in the umbilical region, and one in the right hypochondrium. Occult blood was detected in the stool of 15 patients. About half of these patients were vegetarians. Seven gave a history of hematemesis. Radiologically, 19 showed an ulcer niche, 19 had a deformed and/or an irritable duodenal cap, and 1 had a normal stomach and duodenum.

The patients were given two 5-mg. tablets of oxyphenonium bromide three times a day to start with. No other drug or antacid was given. A bland diet was allowed and no other dietetic restrictions were enforced. Treatment was continued for three to nine months. If the patients complained of dryness of the mouth, constipation, and straining at micturition as most of them did, the dosage was reduced to one tablet four times a day. Nine patients obtained complete relief from pain; 15, over 50% relief; 6, less than 50% relief; and 9, no relief. The ulcer niche disappeared in only three of the eight who reported after eight months of treatment. Probably if this drug is combined with an antacid and used over a sufficient period, the ulcer would show radiologic evidence of healing and the acidity would be reduced in a much higher percentage of patients. In this group the acidity was found to be reduced in 18 patients after three months of treatment.

ISRAEL

Sodium Excretion in Cardiac Patients.—In the early phase of essential hypertension, the hyperexcretion of sodium is a characteristic disturbance. Normal values are reestablished in the later stage of this disease. Since some patients with mitral stenosis develop pulmonary hypertension, Toor and co-workers (*Bulletin Research Council of Israel*, vol. 6, 1957) compared the sodium excretion of these patients, whose mean pulmonary artery pressure ranged from 30 to 75 mm. Hg (group B), with that of those suffering from mitral stenosis whose pulmonary artery pressure was normal (not higher than 16 mm. Hg—group A). A third group (C) consisted of patients with high pulmonary artery pressure and transitory cardiac failure. The serum sodium level was within normal limits in both groups. The average basic sodium excretion in milliequivalents per minute per square meter was 0.21 in group A, 0.55 in group B, and 0.26 in group C. After infusion of 300 ml. of 5% sodium chloride solution, the average excretion of sodium was highest in group B. Groups A and C showed a similar reaction. This suggests that the sodium excretion in patients with pulmonary hypertension due to mitral stenosis is similar to that of those in the early stage of essential hypertension, even if these patients lack any signs of systemic hypertension. Patients with pulmonic and aortic stenosis showed patterns of sodium excretion similar to those found in those with essential and pulmonic hypertension. Toor's investigations suggested that the sodium excretion pattern may be common to quite different conditions and that it is a symptom, not a causative factor.

Lung Cancer.—At a meeting of the Israel Medical Association, J. Rakower reported on the frequency of lung cancer in Israel. The immigration to Israel from many countries in recent years provided a special opportunity to investigate the relative frequency of lung cancer in different communities. At the end of 1954 there were 414,000 Jews in Israel

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who had been born in Asia and Africa, 641,000 born in Europe, and 471,000 born in Israel. The native group was not taken into account because they represented almost exclusively the younger age group with 95% under 30 years of age. In the period 1950 to 1954 the number of deaths from lung cancer per 100,000 population rose from 6.9 to 8.5, but the rate for European-born Jews rose from 11.2 to 16.7, while that for Asian and African-born Jews rose from 3.1 to 5.1.

The assumption that the use of cigarettes at an earlier age may predispose to the development of lung cancer might explain this difference. Furthermore, in Arab countries and among the Arab population the smoking of the water pipe was more popular than the use of cigarettes. It is true that after the immigration to Israel the African and Asian population promptly adopted cigarette smoking. The highest mortality from bronchial cancer among Asian immigrants was found among the Turkish-born. Among Jews immigrated from Yemen, the southern part of the Arabian peninsula, lung cancer is very rare. In the 10-year period 1940 to 1950, no Yemenite Jew was admitted to the Hadassah University Hospital in Jerusalem with lung cancer, and from 1950 to 1954 only six such cases were found in this group. It is interesting to compare the mortality from bronchial cancer of this group with that of the Bulgarian Jewish community, which immigrated to Israel in 1948-1949 as a closed group. The death rate from bronchial cancer in this group of those 45 or older was 27.4 per 100,000 compared to 4.2 for the Yemenite Jews. The mortality rate from lung cancer among Jewish women of European origin reached 10.8 per 100,000 in 1954 and may be considered as one of the highest in the world.

Myocardial Infarction.—In Israel arteriosclerotic heart disease has caused between 9 and 14% of all deaths in recent years. It has been assumed that heart diseases are prevalent in Ashkenasi Jews whereas Oriental Jews are less affected. Dreyfuss and co-workers analyzed a series of 1,020 patients with myocardial infarction and found that 94% belonged to the Ashkenazi, 3.3% to the Sephardic, and 2.3% to the Oriental group. The prevalence of myocardial infarction in Ashkenazi Jews and the rarity in Oriental Jews was thus confirmed.

SWEDEN

Lung Cancer and Tuberculosis.—Dr. A. Westergren (*Nordisk medicin*, Dec. 19, 1957) said that only a few years ago it was rare for primary lung cancer to occur in tuberculous lungs but in 1954 he had observed 10 such cases. He has now made a special study of the 100 patients with primary lung cancer coming to his hospital since 1944. In 33 of these the cancer has developed in a part of the lung which had previously been the site of a tuberculous process. In all but 10 of these patients the tuberculosis might still be active as judged by the finding of tubercle bacilli. In another 11 of these patients there was at least a possibility of an association of tuberculosis with cancer, and it was only in the remaining 12 that such an association was not likely. One reason why this association has been so often overlooked in the past at autopsy may be that in its growth on the site of a tuberculous lesion a cancer may have destroyed such a lesion. Another reason may be found in the observation that tuberculosis has become more common among old persons who are more likely to develop cancer than their juniors. If cancer develops in tuberculous lesions, whether active or inactive, the great increase in the frequency of primary lung cancer may in part be due to the pulmonary tuberculosis of the aged and not exclusively to carcinogens in the inhaled air.

Poliomyelitis Vaccination.—In the spring of 1957 some 660,000 schoolchildren, a limited number of army recruits, and members of hospital staffs were given free of charge two injections of Swedish or American poliomyelitis vaccine. During the school vaccinations, samples of blood were taken from 2,500 children with a view to determining the potency of the different vaccines. Both the foreign and the Swedish vaccines were found to give a good antibody response to poliomyelitis virus type 2. The more dangerous types 1 and 3 showed a less satisfactory response to the American vaccine. After two injections of it, only 38% of the children were found to be immunized to type 1, and only 25% to type 3. The Swedish vaccine gave somewhat better results. None of the children given two injections developed poliomyelitis, but it should be noted that cases of this disease were also rare among persons not vaccinated. The comparatively subordinate role played by the Swedish vaccine in 1957 reflected the shortage of it in the spring of that year. Thanks to the increased supply of it at the present time, it is hoped that in 1958 Sweden can fulfill her domestic needs in this respect.

Glass Blowers' and Trumpeters' Emphysema.—Certain textbooks teach that glass blowers and players of wind instruments are prone to emphysema. Hävermark and Lundgren (*Svenska läkartidningen*, Dec. 13, 1957) addressed a questionnaire to 465 musicians with regard to their respiratory ailments, dyspnea on exertion, and weight. Answers were obtained from 364 (75%). These included 187 blowers of various musical instruments and 159 who had given up using wind instruments. The average age of the blowers was 35 years and the average duration of their musical careers was 18 years. The average age of the nonblowers was 38 years. Dyspnea was, if anything, less common among the blowers

than among the nonblowers. The frequency of dyspnea was about the same for the blowers as for workers of the same age in various other occupations. In another series of tests, 14 musicians using wind instruments and 16 glass blowers from two glass-blowing industries were subjected to various clinical examinations. They included roentgenograms of the chest and spirometric and exercise tests. Here, again, no support could be found for the teaching that emphysema can be provoked by the above-mentioned occupations.

Psychogenic Rheumatism.—Dr. G. Edström, (*Nordisk medicin*, Dec. 19, 1957) stated that the myalgias constitute a variety of ailments with more or less diffuse pain in the muscles as a common factor. If careful physical examination fails to disclose the true nature of the disease, the patient should be questioned as to the possibility of some psychic stress or conflict. In such patients barbiturates or scopolamine with caffeine are apt to be disappointing, whereas modern tranquilizers may give relief. Edström does not believe, however, that psychogenic rheumatism is as common as some, Tegner for example, have suggested.

Spontaneous Pneumothorax.—Dr. S. Bergkvist (*Svenska lækartidningen*, Jan. 10, 1958) reported a series of 44 patients with spontaneous pneumothorax. With four possible exceptions, there was no evidence of tuberculosis in these patients whose ages ranged from 11 to 64 years. Only seven were women, and only in five could a history of straining account for the pneumothorax. Of the 34 patients undergoing a thoracoscopic examination, 17 showed signs of emphysema. The thoracoscopic findings were obscure or frankly negative in seven. While 12 patients received conservative treatment only, the rest were treated by continuous aspiration supplemented in some by the injection of a 5% solution of silver nitrate or a 1% solution of chlortetracycline with a view to promoting adhesions. A 2% solution of chlortetracycline produced shock. Bergkvist emphasized the importance of discriminating in the choice of treatment for a condition that usually ends in spontaneous recovery, since the literature indicates that in 70% the lesion did not recur. It is only under special conditions that treatment designed to provoke adhesions should be used.

UNITED KINGDOM

Fog and Bronchitis.—Waller and Lawther (*Brit. M. J.* 2:1473, 1957) observed a group of 180 patients with chronic bronchitis and emphysema living in the Greater London area. These patients with an established diagnosis of chronic bronchitis and emphysema, who were attending a special clinic at St. Bartholomew's Hospital, recorded their own assessment of their pulmonary condition every day. This assessment was based on a scheme drawn up by the investigators. Daily measurements were made of smoke and sulfur dioxide in the air of central London. A close correlation was observed between the exacerbations of bronchitis and the amount of smoke in the air. In general, the patient's condition began to deteriorate as soon as the concentration of smoke rose and when visibility was reduced. The patients took several days to recover after an attack. The concentration of sulfur dioxide and sulfuric acid rose with that of the smoke and was thought to be partly responsible for the effects observed on the patients.

Brucellosis.—Williams and co-workers reported the first case of human infection by Brucella suis (American type) in the British Isles (*Lancet* 2:1203, 1957). The patient, a boy of four, contracted the infection while on a farm in Erie. The symptoms were pyrexia, enlargement of lymph glands, and splenomegaly. A blood culture yielded Br. suis and agglutination tests were positive at a dilution of 1:1,280. The infection responded to chlortetracycline. There were cows on the farm and the patient drank unheated milk from them. If infection of livestock by Br. suis becomes established in the British Isles, the consequences for agriculture and for public health might be serious.

Kuru.—A new disease known as kuru by the local inhabitants in New Guinea is described by Zigas and Gajdusek (*M. J. Australia* 2:745, 1957), who examined 154 patients with this condition. The first symptom is locomotor ataxia, followed about a month later by tremor, aggravated by excitement or fatigue, affecting the trunk, head, and extremities. Most patients manage to walk with a cane for one or two months and thereafter become sedentary. After some months, unable to sit up, the sufferer develops urinary and fecal incontinence, decubitus ulcers, strabismus, and dysarthria and dies three to six months later. The mind is not impaired, although quite early the patient becomes overemotional, excessive laughter alternating with depression. Towards the end the patient becomes withdrawn and develops a Parkinson-like facies. The main physical signs are a positive Romberg's sign, dysarthria, dysphasia, and incoordination. There is no pyrexia, loss of weight (until the patient is unable to feed himself), and the blood, spinal fluid, and urine appear normal. At autopsy there is widespread neuronal degeneration, particularly in the cerebellum and extrapyramidal system, with lesser destruction of nerve cells and neuronophagia in the anterior horn cells, inferior olives, and thalamus. No treatment appears to be effective. The disease has only been observed among the Fore tribe in a limited area of the eastern highlands of New Guinea. This tribe numbers 16,000 and about 1% are affected. Kuru does not prevent or termi-

nate pregnancy and the infants of mothers suffering from it are unaffected. The disease is attributed to sorcery and after each death a victim is found and made the subject of a ritual murder. The cause is unknown, although a genetic predisposition is likely.

Optic Nerve Injury.—A patient operated on for the removal of nasal polyps brought an action against the surgeon and the Manchester Regional Hospital Board for damages. She claimed that during the operation her optic nerve was damaged. When she awakened from the anesthesia her right eye was swollen, and two days later vision failed. Four days after the operation the eyeball had the appearance of "red jelly" and finally the sight of the right eye was completely lost. The plaintiff claimed negligence on the part of the hospital staff in not reporting the serious condition of her eye earlier. Against the surgeon it was alleged that he had caused injury to the right optic nerve, or bleeding into the orbital tissues resulting in blindness, during removal of the polyps. It was claimed that he should have been aware of this possibility and should have dealt with it when it arose, and should have warned the hospital staff of its possibilities and dangers. A surgeon called on behalf of the plaintiff, admitted that he had come across only two cases of this complication in the literature. He did not think that the occurrence of bleeding behind the eye indicated lack of skill on the part of the surgeon, but he had himself drawn attention to its possibility in a paper in 1955. The surgeon said that he had performed hundreds of operations of this nature, and he was not aware of the possibility of bleeding into the orbit as a complication. An ophthalmologist said in evidence that bleeding into the orbit must be a rare complication, could not be reasonably anticipated, and could not be prevented. He also stated that decompression of the orbit in this case might have done more harm than good. The judge found that there was no lack of care on the part of the surgeon or negligence by the hospital staff.

Hematite Pneumoconiosis.—The deposition of iron oxide in the lung, known as siderosis, and found among knife grinders, silver polishers, electric arc welders, and iron ore miners, was long considered harmless and not accompanied by fibrosis. Faulds (*J. Clin. Path.* 10:187, 1957) from studies of miners in the iron-ore industry of Cumberland, where crystalline hematite is mined, showed that progressive massive fibrosis does occur among these miners. He showed that it is a modified form of infective pneumoconiosis, with a high incidence of associated tuberculosis and lung cancer. Autopsy of 58 hematite iron-ore workers revealed that 30% died from pulmonary tuberculosis, suggesting that the inhalation of hematite dust predisposes to tuberculous infection. The incidence of carcinoma in the 58 autopsies was 12%, which is high in the 1,000 iron-ore miners employed in this locality. The tumors were located in areas of dense fibrosis. Another lesion seen was a lymphadenitis of the hilar glands, with an associated sclerosing bronchitis and ulceration into a bronchus. The development of tuberculosis and lung cancer is a slow process, the average age at death being in the late 50's and early 60's respectively. It is to be expected that the morbidity and mortality from these diseases in iron-ore miners will decrease with the introduction of measures to suppress dust.

Encephalomyelitis Simulating Poliomyelitis and Hysteria.—An endemic occurrence of encephalomyelitis in northwest London, simulating poliomyelitis and hysteria, was reported by Ramsay (*Lancet* 2: 1196, 1957). Thirty-four patients were hospitalized, those admitted in the early stages being given a diagnosis of poliomyelitis, while those conditions that were seen late were invariably diagnosed as functional or hysterical. Further observation revealed that these diagnoses were incorrect and that the patients were actually suffering from a form of encephalomyelitis. The onset of the infection was generally insidious; headache and giddiness were the most constant and striking symptoms. Other symptoms in order of frequency were pains in the limbs, neck, back and chest; shivering and chills; paresthesias; anorexia, nausea, and vomiting; pains in the ears; tinnitus; visual disturbances; and muscular cramps and twitchings. The physical signs, rather than the symptoms, distinguished the outbreak from poliomyelitis. Complete flaccid paralysis and muscle wasting were never present. More striking features were the presence of tendon reflexes, which although sometimes initially depressed were later normal or even exaggerated; sensory impairment for weeks or months; widespread deep muscular tenderness, clonus, and tremor; upper respiratory infection; conjunctivitis; nystagmus, lymphadenopathy; and cranial nerve paresis. A neutropenia with inconstant abnormal lymphocytosis was characteristic of a virus infection. The spinal fluid was normal in all but two patients. The patients with neurological involvement usually recovered slowly. Many of them, however, when grasping objects reported that they tended to drop them. The etiological agent of this condition remains unknown.

Outpatient Psychiatric Service.—In 1956 Graylingwell Mental Hospital in Chichester undertook experimentally to provide an outpatient and domiciliary treatment service for an area covering about 150 square miles with a population of 160,000. Patients were referred to the service by their family physicians. In the first 10 months the service dealt with 1,192 patients (376 men and 816 women), of whom 1,110 were new cases. Nearly 25% were 65 or over. Over 1,000 domiciliary visits were paid by

psychiatrists to 432 patients. Extreme care was used in physical treatments. Each patient first had a thorough physical examination and a comprehensive laboratory investigation before commencing treatment. Electroconvulsion therapy was used extensively among the outpatients, the courses averaging five treatments. Modified insulin therapy was also used. Individual psychotherapy was the main treatment for many patients, and a weekly session in group psychotherapy was also held. Drug abreaction was used in 29 patients. As a result of this extensive outpatient treatment, admissions to the main hospital fell by almost 60%, and by 77% in a neighboring mental hospital. Elderly patients are especially reluctant to enter a hospital, and outpatient treatment proved effective in these patients. The commonest psychiatric illness among these patients was depression.

This experience conclusively showed that for a large proportion of psychiatric patients hospitalization is unnecessary, and that outpatient treatment is entirely effective. Hospitalization is reserved for selected patients only, chiefly those with a good prognosis, but needing special treatment and conditions that cannot be supplied by an outpatient service. The scheme showed that it is not essential, as formerly thought, for psychiatric patients to be removed to the environment of a mental hospital and to be placed under control. The success of such a scheme demands good public relations, cooperative patients, and a favorable home background. The commonest risk is that of suicide by a depressed patient, and in such cases the risk must be weighed. As most mental hospitals in Britain are overcrowded, the Graylingwell Hospital scheme will probably be extended.

Chest Radiography and Radiation Hazards.—The increase in the diagnostic use of x-rays has been particularly evident in chest radiography. Clark and Grenville-Mathers (*Lancet* 2:1276, 1957) were perturbed at the relatively frequent exposure of young people to irradiation in chest clinics. Although the amount of radiation received during chest radiography is small, about 0.38 r for adults and 0.19 r for children, there may be genetic risks, as the dose received by the gonads is 0.36 mr for the male and 0.07 mr for the female and fetus. Since the total dose to the gonads from natural sources of radiation is about 0.15 r each year, the frequency of chest radiography in young persons becomes important. About 4.5% of the boys and 9.3% of the girls under 5 years of age in the authors' chest clinic had had a chest film taken within a year. Among persons aged 15 to 24 attending the clinic only 33% had not had a previous chest film, and nearly 25% had been x-rayed within the previous year. The dose received by children is important, since a comparatively small dose is responsible for the induction of tumors in them, in contrast to the large doses needed in adults. In considering genetic effects it is only the irradiation received by the gonads up to and during the reproductive period that is important.

As many of the patients are referred by general practitioners, and often only as a routine precaution, the author believes that the figures they quoted may be typical of a large section of the population. The risk in x-ray examination must be balanced against the possible advantage, or even necessity, of the examination to the patient. The risk can be reduced by keeping the reexamination rate of such patients to a minimum and by limiting the x-ray beam to those parts of the body that have to be exposed.

Prophylaxis of Rheumatic Fever.—The Rheumatic Fever Committee of the Royal College of Physicians, London, stated in its annual report that in 1956 there were 208 deaths in England and Wales directly attributable to rheumatic fever, and there were 8,208 deaths from chronic rheumatic heart disease, mostly in persons under 35. This represented about 1 death in 2,500 people from this cause in this age group. The report stated that acute rheumatism and its recurrences were the result of infection with the beta-hemolytic Streptococcus of the Lancefield group A, and that recurrences could be prevented by prophylactic treatment with penicillin or a sulfonamide. The Committee recommended that (1) penicillin be given for five years, or until leaving school, whichever is longer, to all who have had rheumatic fever, (2) anyone who has had rheumatic fever and is subsequently hospitalized, or enters a semiclosed community such as a camp, college, or institution, receive preventive treatment, and (3) streptococcic infection occurring in a person who has had rheumatic fever be immediately treated with bactericidal amounts of penicillin. The continuous penicillin treatment was not always successful in the past owing to parental apathy and lack of supervision. The general practitioner should give encouragement, but it is difficult to ensure that children receive penicillin for years when they have no obvious illness. This difficulty can be overcome to some extent by administration of monthly injections of a long-acting penicillin. Some general practitioners object to this procedure because they are afraid of making children hypochondriacs and state that the disease is so uncommon that these precautions are unnecessary. The committee, however, believes that the general practitioner is the key person in the prophylaxis of rheumatic fever. Without his enthusiasm and cooperation it must fail. The type of penicillin treatment suggested is 200,000 units of crystalline penicillin G tablets twice daily, or 120 mg. of phenoxymethyl penicillin (penicillin V) twice daily. Alternatively a monthly intramuscular injection of 1.5 mega units of benzathine penicillin may be given.

CORRESPONDENCE

IMMUNIZATION OF INFANTS WITH POLIOMYELITIS VACCINE

To the Editor:—I should like to comment on the routine immunization of children with poliomyelitis vaccine. The excellent guest editorial by Thrupp (*J. A. M. A.* 166:160 [Jan. 11] 1958) cites data which "suggest that immunization with poliomyelitis vaccine be started in infants as young as six weeks of age." Also, the editorial quotes the American Academy of Pediatrics committee on control of infectious diseases as follows: "It seems reasonable to begin primary immunization (against poliomyelitis) as early as the second month of life." Since immunization with poliomyelitis vaccine should now be routine for all children I would like to suggest its incorporation into accepted immunization schedules. This has several advantages, not the least of which is the avoidance of disruption of the present generally accepted schedule which begins at three months. A suggested addition of poliomyelitis vaccine to a recommended schedule follows (at present the DPT and poliomyelitis vaccine are given at the same time but by use of different sites and different syringes. They are effective if mixed, but as a rule it is best to use mixtures of antigens prepared by pharmaceutical manufacturers because of the possibility of incompatibilities between preservatives and adsorptive agents used by the different manufacturers): 3rd month, diphtheria and tetanus toxoids and pertussis vaccine combined (DPT) plus poliomyelitis vaccine; 4th month, DPT; 5th month, DPT plus poliomyelitis vaccine; 6th month, smallpox vaccination (anytime 1st year); 12th month, DPT plus poliomyelitis vaccine; 24th month, poliomyelitis vaccine; 36th month, DPT plus poliomyelitis vaccine; 60th month, DPT plus poliomyelitis vaccine, repeat smallpox vaccination. (Re: 36th and 60th months: At present a schedule for booster injections of poliomyelitis vaccine cannot be given. It does appear that booster injections will be indicated.)

By simply adding poliomyelitis vaccine at the 3rd, 5th, and 12th month as indicated, immunization against diphtheria, pertussis, tetanus, and poliomyelitis will be achieved simultaneously without inconvenience or extra expense to the parents. We have had such a schedule in effect in our well-baby clinics ever since poliomyelitis vaccine supplies permitted. There is no good reason to disrupt the present schedule by beginning poliomyelitis immunization before 3 months of age.

The optimum schedule for fourth and subsequent (booster) injections of poliomyelitis vaccine has not been established, but it seems very likely that boosters will be needed, particularly if the disease is controlled so well that subclinical infections become rare. There is another very good reason for incorporating poliomyelitis immunization into the present schedule. It seems certain that in the near future routine immunization will employ a quadruple vaccine (DPT plus poliomyelitis vaccine). We have such a quadruple vaccine on trial at present (Quadrigen).

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ROUTINE USE OF CATHARTICS

To the Editor:—I should like to comment on the article "Current Status of Therapy of Infectious Hepatitis" which appeared in the Nov. 30, 1957, issue of The Journal, page 1696. It is not uncommon these days to see parallel articles on the treatment of infectious hepatitis where experts disagree on some fundamentals. This article presents one statement that probably would not be supported by most modern physicians. I refer to the following statement: "Bowel regulation is maintained by saline cathartics in the morning before breakfast and by cleansing enemas." There is no good evidence to support the need for daily or near daily stools in this or any other patient, with the possible exception of those having organic intestinal disease that tends toward fecal impaction or those undergoing medication that will do the same. The average patient with infectious hepatitis falls in neither of these categories.

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PAVLOV AND STAMPS

To the Editor:—In the Jan. 4, 1958, issue of The Journal (page 78), is a foreign letter from the United Kingdom in which the unnamed correspondent holds forth on medical postage stamps, stating that, although Benjamin Franklin "is portrayed on a Russian stamp issued in 1956," "Pavlov has not been pictured on any Russian Stamp." That statement is incorrect: two stamps, showing Pavlov, were issued by Russia in 1949, the centenary of Pavlov's birth. They are in denominations of 40 kopecks and one ruble, and are duly listed in Scott's Standard Catalogue of Postage Stamps, as Russian stamps 1390 and 1391.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Narcotics: Removal of Drug from Body Cavity: Constitutional Problems.—The defendant was prosecuted and convicted for illegally importing and concealing narcotics. From such conviction he appealed to the United States court of appeals for the ninth circuit.

When the defendant walked across the International Boundary Line at the San Ysidro, California, port of entry, he was stopped for interrogation. After removing his coat, at the request of the customs agent, a number of puncture marks in the veins of his arms were revealed. He was then asked to disrobe entirely. Further examination and interrogation revealed that the defendant was concealing a tablespoon of heroin, which was encased in a rubber condom in his rectum. He was asked to attempt to remove the package by forcing a bowel movement. When this was unsuccessful, the defendant was arrested and taken to the San Diego County Jail. There, a physician attempted manual removal of the object but the defendant refused to cooperate by bending over. He was then taken to the United States Naval Hospital at San Diego where two corpsmen were required to exert the necessary force to bend the defendant's body so that his trousers and shorts could be removed and an inspection made by another physician. In attempting to remove the object with the aid of an anoscope and forceps, this physician tore a portion of the outer condum surrounding the narcotics. This gravely alarmed the defendant, who then cooperated willingly. After a number of enemas were administered under the physician's direction and supervision, the heroin, within an inner and outer rubber sheath, was finally recovered. At the trial of the case, the defendant moved to suppress this evidence on the ground that his rights under the fourth and fifth amendments had been violated. The motion was denied and the only question on appeal was whether such rights had been transgressed by the participation of federal law enforcement officers in two separate attempts to effect the removal of the narcotics.

The fourth amendment, said the court, safeguards the right to be free from unreasonable searches and seizures; the fifth amendment guarantees the individual against being compelled to give evidence against himself and also assures to him, under the due process proviso, fair and humane treatment by federal law enforcement officers. There is an ancient exception to the search and seizure prohibition of the fourth amendment, continued the court, and that is the right to search the person of an individual incident to a lawful arrest. The arrest of the defendant was lawful. The tell-tale needle marks and defendant's admission that he had been convicted of using narcotics and that he was carrying narcotics, leave no doubt as to the legality of the arrest. The customs officer, in fact, would have been derelict in his duty had he not done as he did. Having arrested the defendant, the officers were entitled to search his person and to retain incriminating evidence uncovered by the search.

Is there, the court then asked, any fourth amendment restraint on the nature and extent of the search of a person made incident to a lawful arrest —must the search and seizure itself accord with a standard of reasonableness more stringent than the due process limitations? The court noted that where the issue involves the premises and possessions of the person arrested, as distiguished from his person, it has been held that the search and seizure, though incident to an arrest, must not go beyond what is reasonable under the circumstances. Can it possibly be said that it is the command of the fourth amendment that officers act reasonably in searching property, but not so in searching a fellow human being? We think not, concluded the court; therefore we must apply the test of reasonableness to the conduct of the officers in the case at bar.

There is no slide-rule formula yet devised for ascertaining whether specific conduct is or is not reasonable, said the court. Each case must turn on its own relevant facts and circumstances. Here, the defendant was treated civilly throughout and was subjected to physical pressure only when the examinations were to be performed. The officers made no attempt themselves to force the evacuation of the object. The officers had almost incontrovertible proof that the defendant had secreted narcotics. They knew specifically what the defendant had concealed, where it was and how much there was. They knew because the defendant had told them. His admission was corroborated by the presence of a greasy substance around the rectum. As to the actual physical examinations, the court continued, they were conducted by qualified physicians, under sanitary conditions, with the use of medically approved procedures. This kind of examination is a routine one which countless persons have undergone. It is an uncomplicated and nonhazardous procedure. It normally is not painful to a healthy person. Pain results only when the patient refuses to cooperate fully, as the defendant did here. Consequently, whatever pain the defendant endured was due to his actions in attempting to impede the examination. It was self-inflicted. The officers did not exert more than the least amount of force necessary to enable the doctors to examine him. There is not the slightest suggestion in the evidence of threats or attempts to beat or strike him.

In further judging the reasonableness of the conduct, continued the court, it is important to determine the necessity for the action and what, if any, alternatives were presented. What could the officers do in the absence of the defendant's consent? If they simply jailed the defendant, his attorney would have sought his release by way of a writ of habeas corpus. If the writ were granted, the defendant

would walk out with the diacetylmorphine. If no writ were sought, or if one were denied, it would be necessary for the jailers to watch the defendant day and night in order to prevent the evidence from being expelled and destroyed or consumed. The officers would aid what is daily sought to be avoided, the taking of narcotics inside jails and institutions. What an intolerable burden that would cast upon peace officers and jail administrators. Does the Constitution compel this result? Are the hands of law enforcement officers so tightly bound that they must institute a system wholly impracticable and unworkable or else permit the culprit to escape? Is it constitutionally necessary to sacrifice the abiding interest of all citizens of the United States to be free and safe from these insidious drugs in order to avoid offending the sensibilities of admitted narcotic importers? We cannot so read the Constitution, said the court of appeals. There is nothing in the Bill of Rights which makes body cavities a legally protected sanctuary for carrying narcotics. It is not per se violative of the Constitution to remove foreign matter from body cavities, any more than it is to force a person with narcotics in a clenched fist to open his hand. It is necessary to inquire into the particular circumstances to determine whether, in the precise case before the court, the search and subsequent seizure are unlawful. Here the facts not only do not require us to reverse the judgment of the district court, concluded the court of appeals, but encourage us to affirm it. The precise knowledge of what and how much was where, the use of only slight force, the handling of the examinations by qualified doctors, with the use of scientific procedures, and under sanitary conditions, all militate against finding this search and seizure to be unreasonable. The search and seizure not being unreasonable, it follows that there was no violation of the prohibitions of the due process clause of the fifth amendment.

There remains to be considered, said the court of appeals, yet another part of the fifth amendment. The pertinent proviso states that "No person . . . shall be compelled in any criminal case to be a witness against himself." This is the privilege against self-incrimination. Historically and analytically the privilege is confined in scope to testimonial compulsion. The privilege protects one only against extracting from the person's own lips an admission or confession of guilt. The distinction between testimonial compulsion and real evidence taken from the person of the accused is one drawn by both the courts and the writers. The privilege has never had, nor was it intended to have, application to the removal of real evidence from the person of the accused. Therefore, the taking of evidence forcibly from the defendant's body does not come within the purview of testimonial compulsion. Accordingly, we hold that there has been no infringement of the defendant's privilege against self-incrimination.

The judgment of conviction was accordingly affirmed. *Blackford* v. *United States*, 247 F. (2d) 745 (1957).

Governmental Hospitals: Liability of State for Injuries to Inmate.—This was an action for damages on behalf of an inmate of a state hospital for injuries alleged to have been caused by the negligence of the institution's employees. The case was heard in the court of claims of New York.

Part of the therapy treatment at the defendant institution consisted of dances given for the benefit of the patients. At one such dance, the plaintiff and a male inmate left the dance floor through an unlocked and unguarded door, went up a few steps to an empty 8 by 10-ft. hallway, where they had carnal relations, and then returned to the dance. Their departure from the dance hall, their absence, and their return were not observed or known to those in charge of the dance. It was known, or should have been known, that Colletti, the other inmate, was the plaintiff's "boy-friend," that sex was a factor in the plaintiff's illness, that Colletti had given her candy, and that their affection was apparent.

The plaintiff's first claim for damages was based upon the assault, which resulted in her pregnancy. Although such dances are a proper form of therapy, the court said that such events must be properly supervised by an adequate number of competent hospital personnel. In the operation and management of its hospital, the state is responsible for hazards reasonably to be foreseen and for risks reasonably to be perceived. The escape of the two inmates through an unlocked and unguarded door to the vacant hallway should have been foreseen, and the risk of such a venture should have been perceived. The care and supervision provided at the particular event in which the claimant became involved was insufficient and inadequate. Either there were not enough attendants, or the attendants were lax, careless, and negligent in the performance of their duties. The court held, therefore, that the state was guilty under this first cause of action.

The second ground upon which the plaintiff relied for the awarding of damages was the unlawful performance of an abortion. It appears that the existence of the plaintiff's pregnancy was not discovered until about four and one half months after its inception. After the plaintiff's parents were told of the situation and had left the hospital, the director held a conference with his assistant and the psychiatrist in charge of the "acute medical-surgical" building. He was admittedly under a great strain, upset and disturbed. The three doctors decided that an abortion should be performed on the plaintiff and they signed a statement that "Continuation of pregnancy will threaten the improvement shown and will undoubtedly revive the homicidal and suicidal trends."

The evidence, said the court, does not substantiate this conclusion and the general facts and circumstances do not establish the necessity. The hospital doctors, continued the court, certainly knew of the potential criticism against the institution and its administrators as a result of this incident, and such

a conference, if held at all, should have been carried on by physicians and/or psychiatrists whose only concern was the life of the patient. A therapeutic abortion is the only abortion condoned in New York. It is one artificially induced in order to save a life. The abortion performed on the plaintiff was artificially induced, but was not to save a life. It was not, therefore, a therapeutic abortion. Even consent on the part of the plaintiff or her parents would not legalize, justify, or permit it. As a matter of fact, the parents knew nothing of the abortion until after it had been performed. Furthermore, the plaintiff displayed no tendency or indication of suicide or homicide resulting from this pregnancy, and there was no emergency. The court held that the state was therefore liable for such assault and trespass of the person of the plaintiff and for the negligent actions of its physicians, psychiatrists, and other employees.

Accordingly, there was a judgment for the plaintiff on both of her grounds for relief. *McCandless* v. *State, 166 N. Y. S. (2) 272 (New York, 1957).*

MEDICAL FILM REVIEWS

NEW FILMS ADDED TO A. M. A. MOTION PICTURE LIBRARY

William Harvey and the Circulation of the Blood: 16 mm., color, sound, showing time 36 minutes. Produced in 1957 by the Wellcome Film Unit for the Royal College of Physicians, London. Procurable on loan (service charge $5.00) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

This revision of a 1927 film was produced for the Royal College of Physicians on the occasion of the Harvey Tercentenary Congress. It opens with a prologue giving the history of its preparation in an interesting style and goes on to picture a few details of the background of William Harvey. The development of Harvey's thinking is done partly by explanations of previous thought, including the important contribution of Michael Servetus, and by animated diagrams, showing how the data inevitably led not only to interpretation of the pulmonary circulation but also to the conviction that in the extremities and in the peripheral parts of the body generally there must be fine communication between the smallest arteries and the smallest veins. The presentation of Harvey's conclusion from this mass of information has a dramatic quality that will be appreciated by the attentive audience. Because this film summarizes in so vivid and coherent a manner the physiological facts concerning circulation in man, it could be shown profitably as a part of the regular course in physiology for medical students; it covers an essential aspect of the subject, and its attractive material will add to the interest of the entire course. Its usefulness, however, need not be limited to medical students; it will also appeal to nurses, to many nonprofessional groups, and to high school and college students. An audience of physicians would also gain renewed appreciation of the importance of Harvey's contribution as a physician to human welfare. The use of color and music in this film is in unusually good taste, and the narration is clear and pleasing.

Red River of Life: Part I: 16 mm., color, sound, showing time 28 minutes. Produced in 1957 by the Moody Institute of Science, West Los Angeles, Calif. Procurable on loan (service charge $3.00) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

This film, which deals primarily with the physiology of the heart and the circulatory system, compares the human body with an automobile engine and shows how they both have need of fuel supply and removal of waste. After the function of the red blood cell is discussed, the circulatory system is traced throughout the body while it is explained how every cell is supplied with food and oxygen and aids in the removal of waste. How the valves of the heart work under varying conditions of high and low blood pressure and even shock is seen by means of pictures of the valves in action which were taken with the cardiac pulse duplicator, a machine developed especially for this film. An x-ray motion picture shows a plastic artificial heart valve at work in a patient, and the heart-lung machine is explained. This excellent film is scientifically correct and is unique in that it shows the valve action from the inside out. Photographically and educationally, the film is highly recommended for showing to lay groups and also to medical students and nurses.

The Physician and Emotional Disturbance: 16 mm., black and white, sound, showing time one hour. Produced in 1957 by the Mental Health Education Unit, Smith, Kline, and French Laboratories, Philadelphia. Procurable on loan (service charge $1.00) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

This film is a kinescope recording of the five-state, closed circuit Videclinic program which was presented on May 6, 1957. It is designed to give medical audiences the opportunity to discuss the diagnosis and treatment of psychophysiological syndromes seen in office practice. By linking together the annual meetings of five state medical societies, this program explores the role of the general practitioner in the care and treatment of psychophysiological disorders. Scenes of a general practitioner treating a patient who is undergoing the physical symptoms of a common emotional disorder provide the program's panel with the opportunity to discuss the care and treatment of mild emotional disturbances. Members of the panel are Leo H. Bartemeier, Chairman, C. Knight Aldrich, E. Irving Baumgartner, and C. H. Hardin Branch. This film has been edited so that it can be stopped at suitable points for audience discussion. It is recommended for physicians to help them recognize and care for the emotionally disturbed patient.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Electrocardiogram of the 2-Step Exercise Stress Test. G. W. Manning. Am. Heart J. 54:823-836 (Dec.) 1957 [St. Louis].

Various forms of stress or effort tests have been studied for many years with a view to producing diagnostic abnormalities in the electrocardiogram indicative of inadequate coronary blood flow, but there is a difference of opinion as to what constitutes a positive response in the electrocardiogram after exercise. The author, therefore, studied 200 healthy, fit, young men between the ages of 18 and 24 years for comparison with changes observed in patients with proved coronary artery disease, the cases of 4 such patients between the ages of 39 and 77 years being reported in detail. A single and double 2-step test, in accordance with Master's procedure, was carried out in all persons in both groups. Simultaneous leads, 1, 2, 3, and 5 were recorded. Tracings were taken within 5 seconds and 2 and 6 minutes after exercise, the electrodes remaining in place throughout the procedure. The only valid change in the postexercise tracing that constitutes a positive response is a "flat" depression of the RS-T segment subtending an angle of 90 degrees or more with the vertical and greater than 0.5 mm. below the P-R segment. The depression of the segment persists beyond the immediate tracing to the 2-minute or 6-minute tracing, or even longer, or it may not appear until the 2-minute tracing. A depression, with these characteristics, of 1 mm. constitutes an unquestionably positive response.

The tracing of 1 of the 200 healthy men showed a significant segment depression and was considered to be a positive response. False segment depression in a tracing made immediately after exercise and variations to the T wave were frequent in the normal persons. In patients with proved cases of angina pectoris a "true" depression of the RS-T segment usually occurs with the attack and also after exertion. The exercise stress test is of value in doubtful clinical problems if the response to exercise resembles the findings in patients with proved ischemic heart disease subjected to exertional stress. The degree of stress to which the individual patient should be subjected depends on the case. Graded exposure to exercise up to a double 2-step test appears to be a safe procedure. Ideally, the procedure is to be used as an adjunct to the investigation of doubtful cases of ischemic heart disease. When it is used as a routine procedure in examination for cardiovascular fitness for military, aviation, or other occupational purposes, only obviously positive response in which there is no question of a "true" and important segment depression should be regarded as of any significance.

Classical Haemophilia (AHF) Deficiency and Christmas Factor (PTC) Deficiency as Simultaneous Defects. K.-E. Sjølin. Acta. med. scandinav. 159:7-12 (No. 1) 1957 (In English) [Stockholm].

The author reports on a Danish family with 5 hemophiliacs, 2 of whom died of hemophilia at the age of 1 and 35 years, respectively, and 3 of whom are still alive. Quick's prothrombin consumption time tests and thrombin regeneration tests were performed in these 3 patients. Combined coagulation defects were responsible for the hemophilia in 2 of the 3 patients. The thrombin generation test showed the double defect to be caused by lack of antihemophilic globulin (antihemophilic factor, AHF) and plasma thromboplastin component (Christmas factor, PTC). In plasma samples from these 2 patients, the ability to form thrombin with normal speed was present only when AHF (absorbed plasma) as well as PTC (normal serum) were added. There seemed to be a correlation between the defect in the clotting system and the gravity of the clinical symptoms. One of the 2 patients with the combined defect was markedly crippled by the disease. He had severe hemorrhages in the elbow, knee, and ankle joints, causing permanent deformities in these joints. He had a peptic ulcer with several attacks of hematemesis and had received about 200 blood transfusions. The second of these 2 patients frequently had subcutaneous hematomas and had to be admitted to hospital several times for bleeding episodes. The 3rd patient was deficient only in antihemophilic factor. In contrast to the 2 other patients, he had relatively minor inconvenience from his disease and had only received a single transfusion. The frequency of combined AHF and PTC deficiency has not been determined. The inheritance appeared to be sex-linked and recessive.

The place of publication of the periodicals appears in brackets preceding each abstract.

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Management of Peptic Ulcer with Unrestricted Diet and a New Combination of Therapeutic Agents. L. A. Rosenblum. Am. J. Gastroenterol. 28:507-517 (Nov.) 1957 [New York].

Restricted ulcer diets probably interfere with and delay the healing of ulcers, in addition to producing vitamin and protein deficiencies. This paper presents the results of a 2-fold investigation: (1) the antiulcer effectiveness of a more rational therapeutic combination of antacids, anticholinergic agent, and vitamin C, and (2) the use of this preparation without dietary restrictions in the treatment of patients with ulcers. The antacid-antispasmodic preparation was in tablet form and contained 200 mg. of aluminum hydroxide, 50 mg. of magnesium oxide, 2 mg. of scopolamine methylbromide or methylnitrate, and 10 mg. of ascorbic acid. This tablet and a normal, unrestricted diet was given to 145 patients in whom peptic ulcer had been diagnosed clinically and roentgenologically. All but 3 received ambulatory treatment, being permitted to continue their usual occupations. The 3 exceptions were hospitalized for hemorrhage and were treated in the usual manner until bleeding had ceased. They were then permitted an unrestricted diet and given the antacid-antispasmodic tablet. Treatment was continued for 4 to 20 months.

Relief of symptoms and roentgenologic evidence of healing was obtained in 97% of the 145 patients. The quaternary salts of scopolamine exert a potent and prolonged anticholinergic effect when given orally in therapeutic doses; side-effects are minimal. The addition of vitamin C is desirable. The fact that with the use of the described medication relief of symptoms and healing of peptic ulcer can be achieved on an unrestricted diet represents a tremendous psychological benefit. The patient is permitted to live and eat as a normal individual, without interference with his occupation (which would introduce an element of insecurity); this is a potent force in the treatment of what probably is basically a psychosomatic disease.

Results of an Investigation on the Heredity of Diabetes Mellitus. M. Lamy, J. Frézal and J. de Grouchy. Rev. franç. étud. clin. et biol. 2:907-919 (Nov.) 1957 (In French) [Paris].

The authors report on 501 patients between less than 1 and more than 70 years of age with diabetes mellitus and on the families of these patients. Eighty-three of the 218 male patients were under 30 years of age, and 135 were over 30 years of age. Ninety of the 283 female patients were under 30 years of age, and 193 were over 30 years of age. The incidence of the disease was about the same in boys as in girls, but among the adult patients men were outnumbered by women, particularly among those between the ages of 40 and 59 years. No correlation was observed between the maternal age or parity and the incidence of diabetes mellitus. The familial incidence was the same for primary diabetes, i. e., diabetes detected unexpectedly, and for secondary diabetes, i. e., that preceded by an endocrinopathy, particularly a thyroid disorder, pregnancy, trauma, infection, and an emotional upset. Thirty-one fathers and 35 mothers of the 1,002 parents (6.6% of the parents) had diabetes mellitus. The incidence of diabetes was higher among the parents of patients with late diabetes, and that probably may be explained by the fact that the parents of patients with late diabetes were of more advanced age than those of the juvenile patients. Fifty-three (3.1%) of 1,727 siblings, 14 sisters and 10 brothers of male diabetics and 15 sisters and 14 brothers of female diabetics, had diabetes mellitus. The ratio of sisters and brothers with diabetes mellitus, therefore, does not seem to depend on the sex of the proband. Of the 1,727 siblings, 326 were siblings of young diabetics, and 8 (2.5%) of these had diabetes; 1,401 were siblings of patients with late diabetes, and 45 (3.2%) of these had diabetes. The incidence of diabetes in siblings thus was about the same whether the proband was young or had late diabetes.

The following observations were made for relatives of patients with severe, insulin-treated diabetes, independent of the age of these patients at the onset of the disease: (1) consanguineous marriages in the progenitors, (2) diabetes in parents and in both paternal and maternal relatives, and (3) increased incidence of diabetes in siblings if 1 parent has diabetes. The results of this study suggest that the mild diabetes of adult patients would become manifest in heterozygotes because of a gene which would determine in homozygotes a severe diabetes either at an early or at an advanced age.

An Evaluation of Radiology and Gastroscopy in the Differential Diagnosis of Gastric Ulcer. A. E. Dagradi and D. E. Johnson. Gastroenterology 33: 703-713 (Nov.) 1957 [Baltimore].

This study comprises a series of 100 consecutive patients with gastric ulcers (admitted to the Long Beach Veterans Administration Hospital) in whom both radiologic and gastroscopic examinations were performed. Of these patients 65 were subjected to surgery, and pathologic verification of the nature of the gastric ulcer was thus obtained; 35 cases were treated medically, with complete healing of the lesion being observed in almost all instances by both radiologic and gastroscopic control. Ninety-seven of the patients had benign ulcers, 2 had ulcerating lymphomas (Hodgkin's disease), and 1 had a carcinomatous ulcer. The gastroscopic method visualized the ulcer crater in 83 patients and failed to do so in the remaining 17 patients. A correct diagnosis was made in 73, an incorrect one

in 6, and an indefinite one in 4 patients. The radiologic method demonstrated the ulcer crater in 88 instances and failed to do so in 12. Fifty-four correct diagnoses and 15 incorrect diagnoses were made; in 19 patients the diagnosis was indefinite.

Gastroscopic errors were mostly due to the inability of the observer to differentiate inflammatory from neoplastic infiltration surrounding an ulcer crater, with the consequent error in favor of calling a benign lesion malignant rather than vice versa. The gastroscopic method also failed when the lesion was incompletely seen or not seen at all because of its location in a "blind area." Of the gastric ulcers situated on the posterior wall, 41.6% were adequately seen on gastroscopy. Thus one cannot predict on the basis of x-ray localization whether or not an ulcer on the posterior wall of the stomach will be seen gastroscopically. Gastroscopy, though not infallible, is an excellent method for the differential diagnosis of benign and malignant gastric ulcer. X-ray examination and gastroscopic study are complementary procedures. When both methods are applied to the diagnostic study of a patient having a gastric ulcer, the number of patients subjected to surgical exploration because of a question of malignancy as the primary indication will be appreciably reduced; the primary indication for surgery in these patients will then depend on complications of the ulcerative process itself. When an uncomplicated gastric ulcer is deemed to be benign as a result of gastroscopic observation, especially when this finding corroborates a similar x-ray impression, the clinician can elect to pursue a course of medical treatment with a great deal of reassurance.

The Natural History of Polyarteritis. G. A. Rose. Brit. M. J. 2:1148-1152 (Nov. 16) 1957 [London].

The author reports clinical and pathological findings in 111 unselected patients with histologically proved polyarteritis. These findings suggested classification of 98 patients in 2 main groups, i. e., 66 patients, 41 men and 25 women, with polyarteritis nodosa without involvement of the lungs and 32, 16 men and 16 women, with polyarteritis nodosa with involvement of the lungs. This classification stresses the peculiar importance of involvement of the lungs in polyarteritis. It was remarkable that lung lesions, if they occurred at all, almost always preceded lesions in other organs, sometimes by years, and that they were commonly associated with characteristic lesions in other organs, not seen in the patients without involvement of the lungs. At least 3 of the following features were present in each of the 32 patients with involvement of the lungs: a characteristic respiratory illness preceding the onset of systemic polyarteritis, high blood eosinophilia, numerous eosinophils in acute polyarteritic lesions, pulmonary polyarteritis; granulomatous polyarteritis, giant cells in polyarteritic lesions, and the presence of necrotizing or granulomatous lesions, not demonstrably related to arteries, in the liver, kidneys, spleen, lymph nodes, and heart. Microscopically, however, most of the lesions in the 2 main groups were often indistinguishable and the characteristic lesions in patients with involvement of the lungs were often small in number. It is, therefore, not certain whether these 2 syndromes represent distinct diseases or merely variants of the same condition. Suggestive but not conclusive evidence of involvement of the lungs was available in 6 of the remaining 13 patients. The cases of 7 patients differed markedly from both of the 2 main groups; 5 of them were considered as examples of separate diseases which happen to show a similar histological lesion.

The relation between the onset of polyarteritis and preceding respiratory infections was noted before by other workers but received further support. An association with rheumatoid arthritis and with rheumatic fever was also apparent. More detailed evidence obtained in the 111 patients showed that hypertension in polyarteritis nodosa is almost always a result of renal involvement (either arterial or glomerular). Arterial pressure proved to be normal during the acute stage of these lesions and began to rise when healing and fibrosis occurred. The existence of a specific form of glomerulitis with an initial phase characterized by capillary microthrombi, focal fibrinoid necroses, polymorphous infiltration, and capsular proliferation, peculiar to patients with polyarteritis nodosa, was confirmed at autopsy in 16 patients. Hypertension was not a feature of this initial phase. Hypertension and renal failure developed in the 3 patients who survived this stage and died within 1 year. The typical acute glomerulitis was associated with renal polyarteritis in 6 additional patients. The causation of polyarteritis remains obscure. The important observations are the association of some cases with hemolytic streptococcic infections not treated by any drugs, the association of the other cases with rheumatic fever, and the prolonged course of the disease with exacerbations and partial remissions seemingly unrelated to any drug therapy.

Salicylates and Gastric Hemorrhage: II. Manifest Bleeding. H. F. Lange. Gastroenterology 33:778-788 (Nov.) 1957 [Baltimore].

The author's interest in this problem was aroused in 1954 and 1955 when he observed that patients who had received therapeutic doses of salicylates showed a positive benzidine reaction in the feces. In order to obtain a statistical impression of the problem and to discover in which patients manifest bleeding developed, he began this analysis of the connection between aspirin-taking and hematemesis and/or melena, where this was not caused

by hemorrhagic diathesis, varices, cancer, or other causes. Of 96 selected patients, 45 admitted having taken salicylates for varying periods before admittance and immediately before the onset of bleeding. These 45 patients (37 men and 8 women) were compared with 51 patients (37 men and 14 women) who had not taken salicylates. Age distribution was approximately the same in the 2 groups and was similar to that in a group of patients (51 men and 33 women) who were treated at the same time for nonbleeding gastric or duodenal ulcer.

Roentgenologic investigation revealed normal conditions in 20 of 45 persons who had taken salicylates, as compared with 14 of 51 who had received none prior to the occurrence of the bleeding. Seven (19%) of 31 patients with ulcer but no bleeding had taken salicylates prior to hospital admission; these comprised group 1. Twenty-four (37%) of 62 patients with hematemesis or melena proved by roentgenoscopy had taken salicylates immediately before the bleeding occurred; these comprised group 2. Nineteen (56%) of 34 patients with hematemesis or melena not proved by roentgenoscopy had taken salicylates immediately before the bleeding episode; these comprised group 3. The differences between groups 1 and 3 and between groups 1 and 2 are statistically significant. These figures show that the taking of salicylates is a significant factor in provoking gastric hemorrhage. This seems to be particularly true in cases of elderly patients who have been taking salicylates over a considerable length of time.

The Binding of Haemoglobin by Plasma Proteins (Haptoglobins): Its Bearing on the "Renal Threshold" for Haemoglobin and the Aetiology of Haemoglobinuria. A. C. Allison and W. ap Rees. Brit. M. J. 2:1137-1143 (Nov. 16) 1957 [London].

The authors studied specimens of serum from 12 normal persons and from 9 patients with hemoglobinuria. Results confirmed previous findings by other workers that proteins (haptoglobins) exist in human plasma and combine specifically with oxyhemoglobin when the concentration of the latter is up to about 135 mg. per 100 cc. Four distinct haptoglobins, occurring in 3 common and a number of rare combinations, again were distinguished by electrophoretic analysis. The complex of oxyhemoglobin with haptoglobin is relatively stable. When the concentration of oxyhemoglobin in serum or plasma exceeds the combining power of the haptoglobins, however, the uncombined oxyhemoglobin is rapidly broken down, with the formation of methemalbumin.

Experimental work carried out by other workers on dogs and on man has established that when the concentration of hemoglobin in the plasma is below a threshold level no hemoglobin can be detected in the urine. Various concepts have been proposed for the explanation of the renal threshold. The authors suggest an alternative explanation, i. e., that the haptohemoglobin complex probably does not pass into the glomerular filtrate, which free oxyhemoglobin does readily. Hence, hemoglobinuria is observed only when the level of oxyhemoglobin in the plasma exceeds the combining power of the haptoglobins. No haptoglobins could be demonstrated in the serums of 4 of the 5 patients with paroxysmal nocturnal hemoglobinuria and in 2 of the 3 patients with cold hemoglobinuria. The concentration of haptoglobin was considerably below half the normal value in 1 patient with march hemoglobinuria. It is concluded that the susceptibility of these persons to hemoglobinuria is related to the low level or absence of haptoglobins in the plasma.

Cutaneous Staphylococcus Infections in Medical Department: Occurrence of Staphylococcus Aureus Phage Type 80. E. H. Thaysen, K. R. Eriksen and E. Rosendal. Ugesk. læger 119:1381-1388 (Oct. 24) 1957 (In Danish) [Copenhagen].

Investigations on cutaneous Staphylococcus infections in patients and nursing personnel in a medical department were carried out for over 2 years, beginning in the spring of 1954 during an epidemic of furuncles and abscesses among the patients. Most of the infections were caused by phage type 80 stapylococci, which are thought not to have played any conspicuous part before 1954. The infections occurred mainly in elderly, bed-ridden women patients and were apparently transmitted through contact with infected persons and carriers among the personnel. Type determinations of the staphylococci is an essential part in systematic study of the incidence of Staphylococcus infections in hospital wards.

Vascular Changes in Acute Attack of Gout: Favorable Influence of Their Modification. C. Junemann B., R. Domínguez A., R. Barrios and others. Rev. méd. Chile 85:355-371 (July) 1957 (In Spanish) [Santiago].

An acute attack of gout is caused by the abnormal dilatation of the precapillary arteriovenous anastomoses, with consequent dilatation and engorgement of the local veins. The selective location of pain in the joint of the big toe during the acute attack depends on the large number of precapillary arteriovenous anastomoses in that region and on the frequency with which the anastomoses become dilated in the course of gout. Pain appears at first in the limb in which the vasomotor disorder is more marked. Hydergine (a mixture of the three hydrogenated ergot alkaloids, dihydroergocornine, dihydroergocristine, and dihydroergokryptine) con-

tracts the precapillary arteriovenous anastomoses and relieves dilatation and engorgement of the local veins. Eight patients between the ages of 37 and 75 years were treated during an acute attack of gout with Hydergine at the Hospital of the University of Chile. The disease had lasted between 3 and 20 years in these patients. Diet and treatment in common use had failed. The joint of the big toe was the most severely involved. The joints of the tarsus, ankle, knee, elbow, and hand were moderately involved. The treatment consisted in either intravenous or intramuscular injection of 1 cc. of Hydergine in 10 cc. of saline solution, at intervals which varied between 6 and 12 hours, together with 3 or 4 tablets of 0.25 mg. of the drug each with sublingual administration. The treatment was given for a period of 1 or 2 weeks. Oscillometric studies were made before and after the treatment in 4 cases and before and after administration of a first single intra-arterial injection of 2 cc. of Hydergine in 20 cc. of saline solution in 4 cases. The intra-arterial injection of the drug was made into the femoral or the brachial artery. Deformation of the oscillometric curves was observed before the treatment or the intra-arterial injection of the drug in all patients. The degree of deformation of the oscillometric curves was in relation to the intensity of pain. The greatest oscillometric deformation corresponded to the artery nearest the involved joint.

Pain was controlled on the second day of treatment in all patients but 1, in whom pain disappeared on the 8th day of treatment. In this patient, moderate pain appeared after the treatment in another joint and the treatment was considered a failure. The patients could not sleep during the acute attack of gout. They were, however, able to sleep from the first night of the therapy. The temperature and color of the skin over the involved joint became normal. Blood pressure became normal in patients with hypertension; it did not change in patients whose blood pressure was normal before the treatment. The oscillometric curves became normal or nearly normal in all patients, and the subjective and objective symptoms were controlled in all patients.

Nasal Carriage of Staphylococcus Pyogenes by Student Nurses. I. B. R. Duncan, A. M. Collins, E. M. Neelin and T. E. Roy. Canad. M. A. J. 77:1001-1008 (Dec. 1) 1957 [Toronto].

Studies made of the carriage of Micrococcus (Staphylococcus) pyogenes var. aureus by hospital nurses have shown that the carrier rate among them is higher than in the population outside the hospital and that the nurses frequently harbor antibiotic resistant micrococci, particularly strains causing cross infection among patients. The nasal carriage of Micrococcus was investigated in 104 student nurses during the first 8 to 18 months of training and in 15 laboratory workers. Strains found were identified by their antibiotic sensitivity patterns and bacteriophage types. The patterns of carriage in 51 nurses studied intensively were as follows: true carriers, 59% (16% constant and 43% intermittent), and noncarriers and trivial carriers, 41% (35% occasional and 6% noncarriers). The laboratory workers showed similar carrier patterns. Only constant and intermittent carriers demonstrated true carrier status, which was defined as consistent carriage of the same strain for several weeks, and on this basis no real change in carrier rate was observed during the course of the survey even after exposure to ward environment. Antibiotic-sensitive strains decreased from 71% to 13% during the survey and were replaced by other strains, particularly penicillin and tetracycline resistant phage type 81, a strain that was repeatedly isolated from infected patients in the hospital. A larger number of resistant micrococci were encountered in the medical wards than in the isolation wards. No evidence is available regarding the replacement of some micrococcic strains in the nose by others and the fact that noncarriers resist colonization.

SURGERY

Six Months' to Six Years' Experience with Coronary Artery Insufficiency Treated by Internal Mammary Artery Implantation. A. Vineberg and J. Walker. Am. Heart J. 54:851-862 (Dec.) 1957 [St. Louis].

The authors report on 88 patients with angina pectoris due to coronary artery disease who were treated by internal mammary artery implantation and were followed after the operation for 6 months to 6½ years by 2 different groups of cardiologists. The 88 patients were divided into 2 main groups: 68 did not have angina pectoris at rest and their symptoms of angina had been present on an average of 33 months; 20 patients had angina decubitus for an average of 112 months before undergoing internal mammary artery implantation. Four of the 68 patients without angina pectoris at rest died, an operative mortality rate of 5.8%, or about the same as that of patients with angina pectoris who undergo general surgery. Nine of the 20 patients with angina decubitus died, an operative mortality rate of 45%. Thirteen of the entire group of 88 patients died, an operative mortality rate of 14.7%.

Forty-nine (72.1%) of the 68 patients without angina at rest were totally disabled before internal mammary artery implantation; 54 patients (79.4%) returned to work after the operation, and 53 (77.8%) were free of pain or had slight or less pain. There were 4 late deaths 4 months to 4 years after implantation. Sixty (88%) of the 68 patients are still

alive, and 50 (77%) are working. All 20 patients with angina decubitus were disabled, and most of them were bed-to-chair invalids. Since the operation, 7 (35%) of the 20 patients had no pain or less or slight pain and 6 (30%) returned to work. There were 2 late deaths, 9 (45%) are still alive, and 5 of the latter (20%) are at work. The relationship between the duration of coronary artery disease and the ability of the patient to survive and improve after internal mammary artery implantation seems highly suggestive. The optimum beneficial results seem to be obtained in patience who have been suffering, on an average, for 33 months. Excellent results have been obtained up to 45 months. Delay in the surgical treatment of coronary artery disease may result in so much destruction of heart muscle that an attempt at revascularization is futile.

The Role of Digitalis in Mitral Valvuloplasty. B. Burack, J. B. Schwedel and D. Young. Am. Heart J. 54:863-874 (Dec.) 1957 [St. Louis].

The authors report experiences with 50 consecutive patients selected for mitral valvuloplasty in whom the digitalis preparations apparently played a major role in their preoperative and postoperative medical management. The patients were divided into 6 categories, with 1 patient being included in 3 categories. Five patients did not receive digitalis before surgery; 10 received inadequate amounts of digitalis before surgery; 4 were unable to tolerate anesthesia until further digitalis therapy was employed; 26 were given digitalis for prolonged periods before surgery; 4 received digitalis during the preoperative period and were subjected to exploration without valvuloplasty; and 3, who were desperately ill, died, 1 of a massive hemorrhage from a tear in a friable left auricle and 2 others of ventricular arrhythmias which occurred during anesthesia before actual cardiac manipulation. The short latent period induced by lanatoside C and the more prolonged effects of digoxin, together with their relatively rapid elimination, made these agents the drugs of choice.

Auricular fibrillation, often accompanied by congestive heart failure, occurred postoperatively in all patients with regular sinus rhythm who received no digitalis or inadequate amounts of digitalis during the preoperative period. Rapid ventricular rates and congestive heart failure occurred, with but 1 exception, during anesthesia or during the postoperative period in patients with preoperative auricular fibrillation who received short-term or inadequate digitalis preparation. The use of quinidine, unless combined with digitalis, did not prevent the appearance of postoperative arrythmias. The most benign postoperative course was noted in patients who received adequate long-term digitalis therapy. The use of potassium helped to prevent toxic manifestations in patients with an increased digitalis intake. The parenteral administration of digitalis during the immediate postoperative period appeared to eliminate or decrease the amount of nausea and vomiting, as compared to that occurring in patients in whom an attempt was made to administer orally equivalent amounts of digitalis. The patient's ventricular response to exercise during the preoperative preparatory period as an important criterion for adequate digitalization is suggested. The increased need for digitalis subsequent to surgical intervention on the mitral valve may reflect the increased left ventricular filling after valvular fracture, the decrease in stroke volume output consequent to tachycardia, and the positive fluid balance occurring postoperatively.

Long-term administration of digitalis in larger than usual maintenance doses up to 0.75 mg. of digoxin daily affords the myocardium greatest protection against arrhythmias and congestive heart failure in patients undergoing mitral valvuloplasty. It is recommended that all patients have prolonged and full digitalization before mitral valvuloplasty, regardless of the rhythm or lack of evidence of congestive failure.

Pericardectomy for Chronic Constrictive Pericarditis. J. R. Marshall and J. F. Pantridge. Lancet 2:1039-1040 (Nov. 23) 1957 [London].

Of 18 patients with chronic constrictive pericarditis seen in the past 7 years by the authors, 17 have undergone pericardectomy. The earlier patients had only their ventricles decorticated, as it was commonly held that it was unnecessary to decorticate the auricles and that the latter procedure was hazardous and should not be attempted. The slow and often incomplete return to normal of patients who underwent limited pericardectomy, and particularly the experience with a 9-year-old boy who showed the clinical picture characteristic of constrictive pericarditis (effort intolerance, engorged jugular veins, hepatic enlargement, ascites, a third heart sound, and absence of cardiac enlargement) led the authors to doubt the efficacy of decortication confined to the ventricles. In this instance, in which pericardectomy was done with both ventricles being completely decorticated, no significant clinical improvement followed. The central venous pressure remained high (26 cm. saline solution) and hepatic enlargement persisted. At a second operation in which the ventricles were found to be entirely clear, a dense mass of fibrous tissue was removed from the right auricle and vena cava and the venous pressure fell immediately. Several investigators hold that decortication limited to the ventricles is adequate for the complete relief of the hemodynamic disturbances produced by chronic constrictive pericarditis, while others and the case cited indicate that complete decortication not only of the auricles and ventricles but also of

the vena cava is necessary to restore the normal motion of the auriculoventricular ring which is important in the action of the right side of the heart. The object of surgery in constrictive pericarditis should be to restore the normal motility of the auriculoventricular ring in addition to the decortication of the ventricles.

Successful Resection of Fusiform Aneurysm of Aortic Arch with Replacement by Homograft. M. E. De Bakey, S. Crawford, D. A. Cooley and G. C. Morris Jr. Surg. Gynec. & Obst. 105:657-664 (Dec.) 1957 [Chicago].

The 2 major problems associated with resection of aneurysms of the proximal portion of the aortic arch are concerned with the rapidly fatal consequences of arrest of circulation through this vital segment of the aorta on the heart and the central nervous system. Earlier efforts to solve these problems were directed toward use of temporary shunts to provide circulation during excision and replacement of the diseased segment and use of hypothermia to reduce cardiac output and oxygen requirement by the tissue. Although these methods proved to be feasible and to some extent effective in overcoming these problems, they have certain disadvantages that impose additional risks to the operation. Moreover, in some cases in which, for example, the aneurysm arises proximally on the ascending aorta, it is not technically possible to make use of the shunt. These disadvantages have been circumvented by use of temporary cardiopulmonary bypass with the artificial heart-lung apparatus. This method was first successfully employed by the authors about 1 year ago in a patient with an aneurysm involving the ascending aorta, which was resected and replaced with a homograft.

Its successful application in a second patient, a 56-year-old man with a fusiform aneurysm involving both the ascending aorta and transverse arch, is reported in this paper. An artificial heart-lung apparatus using a modified DeWall-Lillehei oxygenator was primed with 6 units of heparinized blood. The superior and inferior venae cavae were mobilized within the pericardial cavity and encircled with umbilical tapes to be used later as temporary tourniquets. After the patient had been given 100 mg. of heparin, a no. 16 tygon catheter was inserted into each vena cava through a small incision made in the right auricular appendage and secured in place by pursestring sutures. A similar catheter was inserted into the common iliac artery through an arteriotomy made in the right common femoral artery, and 2 smaller catheters were inserted into the innominate and left common carotid arteries, respectively, through small arteriotomies made distal to the aneurysm in the thoracic segments of these vessels.

The aortic arch containing the aneurysm was excised and replaced by a reconstituted lyophilized aortic arch homograft, care having been taken to preserve the vagus, recurrent laryngeal, and phrenic nerves. The graft was inserted by anastomosis of the distal aorta and then the left common carotid, innominate, and proximal aorta in that order, using continuous over-and-over through-and-through sutures of 000 silk. At the completion of the anastomoses 150 mg. of protamine sulfate was given, and the bulldog clamps, which had previously been placed on the innominate, left common carotid, and subclavian arteries, were removed, after which the distal and proximal aortic clamps were removed in that order. The tourniquets occluding the venae cavae were immediately released, the pump discontinued, and normal circulation was restored through the heart and lungs. The entire perfusion time was 43 minutes. The operation was completed by removing the perfusion catheters, repairing the mediastinum, and closing the chest wall. Immediately after the operation, the patient responded to questions and moved all extremities. Recovery was essentially uneventful, and the patient was discharged 16 days after the operation. He has since been observed several times, and, 5 months postoperatively, his condition continues to be satisfactory and he has resumed working full time as a carpenter.

Pulmonary Cryptococcosis. S. J. Kuykendall, F. H. Ellis Jr., L. A. Weed and F. E. Donoghue. New England J. Med. 257:1009-1016 (Nov. 21) 1957 [Boston].

Cryptococcosis, also known as torulosis and European blastomycosis, is a subacute or chronic mycotic infection caused by Cryptococcus neoformans (Torula histolytica, Cryptococcus hominis). Although evidence exists that the skin and mucous membranes may be sites of primary inoculation, most authorities agree that the respiratory tract is probably the most common portal of entry of the organisms in human beings. The organisms are thought to be air borne from a reservoir in the soil. The infection may be disseminated hematogenously from any portal of entry to involve any part of the body. There is a marked predilection for metastatic involvement of the brain and meninges, and this is almost uniformly fatal. Occasionally, the disease may be diagnosed while still limited to the lungs, lymph nodes, skin, or eye. Such localized infections are amenable to excisional therapy with the hope of cure before dissemination. The authors present 4 patients in whom apparently localized lesions of pulmonary cryptococcosis were excised surgically. Cryptococcosis limited to the lungs may be asymptomatic, or, when symptoms are present, they may be nonspecific and are usually those of an upper respiratory infection, with mild cough

and scanty mucoid sputum. There may be low-grade fever, malaise, thoracic pain, or loss of weight. As with other mycotic diseases, males are affected more frequently than females. Ages of patients varied from 12 to 71 years, the majority being between 20 and 50 years. There may be moist rales, altered breath sounds, dullness, a pleural friction rub, or pleural effusion. Roentgenologic findings are also variable. The most common early lesions appear to be circumscribed, patchy areas of consolidation of moderate density.

The differential diagnosis usually is between primary or secondary carcinoma, tuberculosis, other mycotic infections, chronic pulmonary abscess, and bronchiectasis. Skin tests and immunological tests are of limited value. The causative organisms may be isolated from the sputum, bronchial washings, and pleural fluid, but the diagnosis of localized pulmonary cryptococcosis is seldom made before surgical exploration. The disease usually runs a benign, slow course until hematogenous dissemination to the central nervous system or elsewhere occurs, and then the course is steadily downhill, death usually being due to meningoencephalitis. Spontaneous regression or disappearance of pulmonary lesions has been reported, but there is always the threat of dissemination of the disease if it is left untreated. Surgical extirpation of the pulmonary lesion before hematogenous spread has occurred appears to be the treatment of choice.

Limitations of Curative Treatment of Patients with Bronchopulmonary Carcinoma. P. Renault and M. Bairon. Semaine hôp. Paris 33:3660-3667 (Oct. 30) 1957 (In French) [Paris].

The authors studied specimens obtained from 450 patients with bronchopulmonary cancer who were operated on. Although the results of surgical treatment are disappointing, this method remains the major procedure in the management of patients with brochopulmonary cancer and provides the only possibility of survival. There remains the problem on what clinical evidence the selection of patients for surgical treatment should be based. Extrathoracic metastases represent a definite contraindication, but they are far from being regularly detected by clinical examination. Cancer of the lung, as most of the other cancers, shows intermittent acceleration of growth, and surgical treatment is contraindicated during a bout of the growth process. Unfortunately, the tests of growth, including the patient's weight, rise of temperature, erythrocyte sedimentation rate, fibremia, and electrophoresis, are neither specific nor reliable; the interpretation of their results is made difficult by the frequent occurrence of superadded infection. Only a peripheral, apparently isolated tumor mass may be of definite significance.

The intrathoracic extension of the tumor is of major importance concerning the possibilities of curative treatment. The round peripheral tumors, which are well limited, are enclosed in an aerated parenchyma, and have a clear radiologic aspect, present the ideal type for surgical intervention. Lobectomy is the method of choice. Spread of the tumor to the hilus of the lung by way of the bronchi may be observed particularly in tumors arising in the major bronchi or in certain infiltrating tumors of the bronchus of the upper lobe. These forms are poor surgical risks. At least 1 cm. of healthy bronchus beyond the bronchotracheal projection is indispensable to provide safe closure of the pneumonectomy stump. The various modes of spread of the tumor by way of arteries, veins, and lymphatics and the involvement of the serous surfaces of the pleura and the pericardium are discussed. Despite the achievements obtained in the development of more perfect roentgenographic and bronchoscopic methods, it is still difficult to obtain an accurate appraisement of the intrathoracic spread of the cancer and of its operability. Exploratory thoracotomy supported by extemporaneous histological examination is, therefore, considered indispensable, provided that its performance is not contraindicated for other reasons.

Lymphangiosarcoma Secondary to Chronic Lymphedema. J. B. Herrmann and J. G. Gruhn. Surg. Gynec. & Obst. 105:665-674 (Dec.) 1957 [Chicago].

The authors add the histories of 5 patients with postmastectomy lymphangiosarcoma to 21 previously reported by other investigators and analyze the data on the 26 patients. Two cases of lymphangiosarcoma of the lower extremity are also mentioned. The mean age of the patients at the time of mastectomy was 51.5 years. The mean age at the time of appearance of lymphangiosarcoma was 62 years. Lymphangiosarcoma occurred most frequently in the patients who had mastectomy and who were apparently cured of breast carcinoma. Evidence of metastatic breast carcinoma was present in only 1 patient, and postmortem examination of 4 patients revealed no evidence of mammary carcinoma. The likelihood of recurrences or metastases decreases as the postoperative interval increases, which is a probable explanation for the mean interval of 10 years between mastectomy and occurrence of lymphangiosarcoma. The microscopic appearance of lymphangiosarcoma was studied and compared with that of Kaposi's sarcoma. The possibility of blood vessel origin of lymphangiosarcoma could not be excluded.

The significance of preceding malignant neoplasia, of irradiation, and of chronic lymphedema as possible predisposing factors was investigated. None could be definitively implicated as the actual causal factor, but all may play a part. The prog-

nosis for patients with lymphangiosarcoma is grave. Most patients died of pulmonary metastasis within 1 year, and no therapeutic procedure proved satisfactory. Four patients survived 3 or more years. Two patients had received radiation therapy only, and 2 patients had undergone interscapulothoracic amputation. It is suggested that irradiation be given as the initial therapy since lymphangiosarcoma is radiosensitive in certain patients. Interscapulothoracic amputation can be considered if no favorable response is obtained within a relatively short time after institution of radiation therapy.

A Five- to Ten-Year Follow-Up Study of the Billroth I and Billroth II (Polya) Operations for Duodenal, Gastric and Gastrojejunal Ulcer and Gastroenterostomy with Vagotomy in the Treatment of Duodenal Ulcer. W. Walters, T. E. Lynn and J. E. Mobley. Gastroenterology **33**:685-690 (Nov.) 1957 [Baltimore].

The essential difference between the Billroth 1 and Billroth 2 types of partial gastrectomy, sometimes referred to as gastric resection, is the anastomosis. In the Billroth 2 procedure or its modifications, the end of the duodenum is closed and the proximal portion of the stomach is anastomosed to the jejunum, usually about 4 or 5 in. from the ligament of Treitz. After this operation, bile and pancreatic and duodenal secretion seep up through the anastomosis into the gastric segment of stomach before passing down the distal loop of jejunum. In this way they assist in the neutralization of the acid gastric secretion from the remaining segment of stomach. In the Billroth 1 operation, the proximal end of the resected stomach is anastomosed to the end of the duodenum and little alkaline duodenal, pancreatic, or biliary secretion seeps into the stomach. At the Mayo Clinic a 5-year to 10-year follow-up study was made on patients with duodenal ulcer in whom gastric resections of Billroth 1 and Billroth 2 types or vagotomy plus gastroenterostomy was performed.

The best results were obtained with the Billroth 2 operation. In the group of patients who underwent this operation, the incidence of excellent and good functional results was highest, the incidence of ulcer recurrence was lowest, and the incidence of dumping or nutritional disturbances was no greater than in the group treated by vagotomy and gastroenterostomy. The mortality rate was approximately the same in all 3 series (1.2-2%). In the patients with gastric ulcer and in the series in which gastrojejunal ulcer had developed after gastroenterostomy, the Billroth 2 operation also gave the highest incidence of good and excellent functional results and the lowest recurrence of ulcer. In a previous study of gastrojejunal ulcers, Walters, Chance, and Berkson showed that the best results in cases of gastrojejunal ulcer developing after gastroenterostomy were obtained with the Billroth 2 type of gastric resection. When the gastrojejunal ulcer developed after an adequate gastric resection had been done, vagotomy gave the best results. In 1955, partial gastrectomy was used for approximately 90% of the patients operated on for chronic recurring duodenal ulcer at the Mayo Clinic; gastroenterostomy was used for 5% and gastroenterostomy with vagotomy for 5%.

Radical Panhysterectomy and Pelvic Node Excision for Carcinoma of the Corpus Uteri. A. E. Schwartz and A. Brunschwig. Surg. Gynec. & Obst. **105**:675-680 (Dec.) 1957 [Chicago].

The policy of radical hysterectomy and of pelvic node dissection has been followed on the Gynecological Service of the Memorial Center for Cancer and Allied Diseases in New York since 1947. While it had been hoped that this method could be used in a larger number of patients each year, several factors limited the group in which the extended procedure could be performed to about 20% of those patients operated on year after year. Since 1947, pelvic node dissections have been done in combination with panhysterectomy or excision of a cervical stump for endometrial carcinoma in 96 patients. The surgical and hospital mortality was 2%. The incidence of urinary tract fistulas was 8%. Pelvic node metastases were found in 13 (14%) of the patients. Two of these 13 patients are alive and well more than 5 years after radical hysterectomy and pelvic node dissection. One is alive and well after more than 2 years. The remainder have died of recurrent disease. It has been stated that, if the endometrial carcinoma involves the isthmus or endocervix, it is more likely to spread to pelvic lymph nodes, because the cancer has entered the lymphatic drainage of the cervix, than if the lesion is situated in the fundus.

The location of the lesion and depth of myometrial invasion of the 13 patients with positive pelvic nodes support this contention. In 11 patients the lesion had extended to the isthmus or endocervix. One of the 2 patients in whom the pelvic nodes had become involved despite the fact that cancer was limited to the fundus survived 5 years. This fact emphasizes the importance of the pathway of lymphatic spread via pelvic nodes when the lesion is present in the fundus alone, as well as when it involves isthmus or endocervix. It is noteworthy that of the 13 patients 7 had metastases involving hypogastric nodes and in 5 patients parametrial nodes also contained metastases.

The 37 patients who were followed up for 5 years or more after pelvic node dissection are divided into groups according to the location of the lesion within the uterus. Of 14 patients whose lesion was located in the fundus of the uterus, 12 survived 5 years or more. Of 12 patients in whom

carcinoma was present in the fundus but involved isthmus or endocervix as well, only 5 survived 5 years or more. The authors gained the impression that the location of the lesion per se is not the most significant factor but rather the depth of myometrial invasion. Thus, the poorer prognosis in the group in which a lesion in the fundus had spread to isthmus and endocervix was also associated with a more advanced lesion, as evidenced by a high degree of deep myometrial invasion. The authors realize that pelvic node dissection constitutes an appreciable extension of the operation, which should not be essayed in a large percentage of patients because of obesity and advanced age. With due consideration of the general status of the patient, however, radical panhysterectomy with pelvic node excision seems to be a logical operation for cancer of the body of the uterus because, if nodes have been invaded, the patient will be given the benefit of their excision. In the absence of detectable metastasis in the pelvic nodes, such an operation is preferable to simple panhysterectomy on the basis of the principle that wide excision should be performed for a malignant lesion.

A Five Year Survey of 1,055 Consecutive Patients With Extrahepatic Biliary Tract Diseases. J. R. Babcock and R. C. Eyerly. Surg. Gynec. & Obst. 105:711-716 (Dec.) 1957 [Chicago].

A total of 1,055 patients with extrahepatic biliary tract disease were analyzed. This group represented 2% of the total admissions to 2 hospitals during that time. Of the 1,055 patients, 768 (72.8%) were operated on. The 768 operations represent 8% of the total number of operations performed during the period of study, 1948-1952 inclusive. Choledochostomy was performed on 24% of the patients subjected to cholecystectomy, calculi being found in 55% of them. Exploration of the common duct did not cause more deaths than cholecystectomy in patients with chronic cholecystitis and cholelithiasis. The mortality rate was 5 times as high after acute cholecystitis with cholelithiasis than after chronic cholecystitis with cholelithiasis. Associated cardiac disease in aged patients contributed greatly to the mortality rate, especially in patients with acute gallbladder disease. Secondary operations on the common duct were not as frequent as reported from many other clinics. There were no deaths after operations in this group. The results were good in all patients operated on for retained stones or stenosis of the sphincter of Oddi. The condition of 50% of patients operated on for stricture of the common duct was improved, the remaining patients have recurrent symptoms which are being treated conservatively.

The over-all operative mortality was 3.4%. The highest mortality occurred in patients suffering from malignant disease of the biliary tract. The most frequent cause of death in this group was metastatic disease and hepatic failure. Deaths were relatively twice as frequent in men as in women. Cardiac arrest was the cause of death in 3 patients, but it is regarded as incidental in these patients and not peculiar to gallbladder disease. This review revealed that the majority of patients with biliary tract disease are over 50 years of age, that most postoperative deaths occur in patients over 50 years of age, and that the mortality can be greatly reduced by earlier diagnosis and by more prompt surgical eradication of the disease.

Generalized Excessive Oozing in Patients Undergoing Major Surgery and Receiving Multiple Blood Transfusions. M. B. Zucker, M. Siegel, E. E. Cliffton and others. J. Lab. & Clin. Med. 50:849-861 (Dec.) 1957 [St. Louis].

The authors report excessive generalized bleeding or oozing in 15 of 78 patients who were undergoing extensive surgery for malignant neoplasm. Blood clotting factors and fibrinolysis were studied in the 78 patients before, during, and after the surgical intervention. Oozing could not be ascribed to massive blood replacement, and in none of the patients in whom oozing occurred was the platelet count below 100,000 per cubic millimeter. Plasma citrate concentration bore no relationship to the occurrence of oozing. Fibrinolytic activity of the euglobulin fraction was found during or shortly after surgery in 9 of the 15 patients. Active whole clot lysis was observed in 6 patients. Fourteen of the 63 patients in whom oozing did not occur had euglobulin fibrinolytic activity, and 5 had whole clot lysis. Fibrinogen concentration fell below 100 mg. per cubic centimeter in only 3 of the patients in whom oozing was found, 2 of whom were undergoing hepatic lobectomy. Decreases in prothrombin and factor 7 concentrations during surgical intervention occurred with equal frequency among patients in whom oozing occurred and among those in whom it did not, but decreases in factor 5 occurred more frequently in patients in whom oozing was seen. Values below 50% of normal were observed only in patients undergoing hepatic lobectomy. All but 1 of 14 patients with oozing for whom adequate data were obtainable showed a change in at least 1 of the factors measured. Three had poor prothrombin consumption before surgery, 3 had prothrombin or factor 5 concentrations below 70 per 100 cc., and the remaining 7 had fibrinolytic activity and in addition some other change. The correlation between oozing and the occurrence of multiple changes was statistically significant.

It is difficult to assess therapeutic measures because both lysis and oozing may cease without treatment. Lyophilized fresh (antihemophilic) plasma was used largely because many of the samples tested had very high antifibrinolytic ac-

tivity. It also contains prothrombin, factor 7, and fibrinogen in approximately normal concentration, but there is a subnormal concentration of factor 5. Fresh whole blood collected in plastic bags is recommended when thrombocytopenia is present, and fibrinogen (fraction 1) should be given when severe hypofibrinogenemia occurs.

NEUROLOGY & PSYCHIATRY

Further Results of New Methods of Treatment for Parkinsonism. F. Giberti, G. Gianniotti and S. Spizzirri. Gazz. med. ital. 116:404-407 (Sept.) 1957 (In Italian) [Turin, Italy].

Sixty-four patients with extrapyramidal syndrome, of whom 13 had Parkinson's disease, 46 postencephalitic Parkinsonism, and 5 other extrapyramidal syndromes, were treated for 60 days with a new Compound 10870, whose chemical formula is 3-phenyl-3 (β-diethylaminoethyl)-2-6-dioxypiperidino-hydrochloride. The patients were divided into 4 groups. The 1st group received regular Compound 10870 alone, the 2nd group long-acting Compound 10870, the 3rd group Compound 10870 combined with reserpine, and the 4th group Compound 10870 combined with reserpine and Ritalin (methylphenidate hydrochloride). Regular Compound 10870 was most effective in improving hypertonia and tremor. Long-acting Compound 10870 improved the vegetative symptoms: hypersalivation, seborrhea, and hyperidrosis. The combined treatment with Compound 10870 and reserpine or Ritalin afforded no benefit to the patients. Worsening of symptoms occurred in a patient with a choreiform syndrome.

The authors began treatment with daily dosages of 1.25 mg. of regular Compound 10870, 0.25 mg. of reserpine, 2.50 mg. of Ritalin, and 3.75 mg. of long-acting Compound 10870, administered in divided doses of 3 to 6 a day. The dosages were gradually increased every 2-5 days until the following maximum tolerance to the drugs was reached: 30 mg. of regular Compound 10870, 6 mg. of reserpine, 35 mg. of Ritalin, and 37.5 mg. of long-acting Compound 10870. The treatment was discontinued in a few patients after 20 to 30 days. Relief of 1 or more symptoms was observed in 36 patients and no relief of symptoms in 28. The greatest relief of symptoms in descending order of frequency and intensity was as follows: hypertonia (40 of 63 cases), tremor (33 of 60 cases), vegetative and psychic disturbances, and speech impairment. Patients with Parkinson's disease derived greater benefit from the drug than those with postencephalitic Parkinsonism. Compound 10870 was well tolerated. Minor side-effects were observed in a few patients: 5 complained of dryness of the mouth, 3 of temporary edema, 3 of mental confusion, and 2 of blurred vision.

Fatal Damage to the Brain by Epileptic Convulsions After a Trivial Injury to the Head. J. M. Small and A. L. Woolf. J. Neurol. Neurosurg. & Psychiat. 20:293-301 (Nov.) 1957 [London].

The susceptibility of the brain in childhood to anoxic damage during epileptic convulsions is still not widely recognized. The authors present the history of a 13-year-old boy who, in the course of a cricket game, was struck by the cork ball on the forehead. The boy had been in good health and had no history of seizures. After he was hit by the ball, he fell over backwards but picked himself up and went on playing as though unaffected. Later he went home with a friend, passed a normal night, and went to school the next day. He behaved normally at school but boasted about the bruise on his forehead. At 4:15 p. m. he returned home, carried out a shopping errand, and seemed in every way normal until 6:15 p. m., when his mother noticed that he appeared to be "unconscious." A few moments later, he got up from his chair with his eyes shut and picked up a piece of bread from the table, put it in his mouth, took it out, and then had a fit, all limbs convulsing, and became unconscious. He was hospitalized at 7 p. m. and later vomited. In the course of the following 2 days he had a series of epileptic attacks followed by deepening unconsciousness and death.

During one of the more severe attacks amounting to status epilepticus, there was evidence of embarrassed respiratory function and accumulation of bronchial secretions. Neurosurgical investigation and subsequent postmortem examination showed that there was no intracranial hemorrhage or other naked-eye findings to explain the deepening unconsciousness. Histological examination of the brain showed widespread, though asymmetrical, cerebral degeneration typical of anoxia. It is pointed out that epileptic convulsions, whether traumatic or otherwise, may cause anoxic damage to the brain. The role of respiratory embarrassment during status epilepticus in producing this anoxia is stressed. The connection between the trivial head injury and the convulsions remains obscure, but a similar case is recorded in the literature.

Kuru: Clinical Study of a New Syndrome Resembling Paralysis Agitans in Natives of the Eastern Highlands of Australian New Guinea. V. Zigas and D. C. Gajdusek. M. J. Australia 2:745-754 (Nov. 23) 1957 [Sydney].

The authors report clinical, pathological, and epidemiologic observations on 154 patients with a new illness resembling paralysis agitans or Parkinsonism and apparently belonging to the group of chronic progressive heredofamilial degenerative disorders of the central nervous system. The patients were natives of the Fore linguistic and cultural group in the Eastern Highlands of New

Guinea and their immediate tribal neighbors who intermarry with them. Twenty-four of the 154 patients were male and 130 female. Of the 49 patients between 5 and 19 years of age, 18 were male and 31 were female. Of the 105 patients between 20 and more than 40 years of age, 6 were men and 99 were women. The disorder affects principally adult females, but almost 25% of the patients are children of both sexes. Adult males are rarely affected. The illness is apparently restricted to the Fore group with a population of about 11,000 and to only those portions of their tribal neighbors, the Kimi, Auiana, Usurufa, Kanite, Keiagana, and Iagaria, who intermarry with them, an estimated additional population of about 5,000. The disease is designated "kuru" by the natives.

The first symptom was locomotor ataxia. About 33% of the patients reported knee pain, headache, malaise, fever, cough, and coryza, in order of decreasing frequency, as prodromal symptoms. As the ataxia became more marked, with awkward placement of the feet and a swaying and weaving gait, a distinctive tremor involving the trunk, extremities, and head appeared, and this tremor was exaggerated when the patient attempted coordinated voluntary motor activities or when he was excited or apprehensive, fatigued or exhausted. Within 1 month of the onset, both the ataxia and tremors were usually prominent. During the second to the third month of illness, when tremors became more severe and rather coarse in quality, a choreiform component entered into the involuntary motor pattern. Most patients continued to walk with the support of a stick for 1 or 2 months and thereafter could no longer maintain their equilibrium unassisted and remained sedentary but still moderately well integrated in their native society. The patients' conditions rapidly deteriorated, and, from 3 to 6 months after the onset, they were left to lie indoors with fecal and urinary incontinence and rapidly developing decubitus ulcers. Convergent strabismus was often present at this time. Speech and intelligence were normal in the early stages, but dysarthria appeared in the 2nd to the 4th month and became more marked as the disease progressed. Still in the early months of illness, marked emotionalism appeared; inappropriate excessive laughter and slowly relaxed smile or paroxysmal hilarity alternated at times with moods of depression and, occasionally, of moderately belligerent or aggressive behavior. Later a gradual pattern of withdrawal, with a mask-like facies resembling that of classical Parkinsonism, was observed. Until late in the illness there was no muscular weakness or paralysis and no rigidity or spasm, and, although in advanced stages severe muscular spasm and intermittent resistance to passive motion of the extremities appeared, muscular contractures were very late in developing despite the predominantly flexed posture which the patients generally assumed and occasionally did not develop at all. The disease usually ran its course in 6 to 9 months and rarely lasted over 1 year.

Preliminary neurohistological examination of 6 of the 10 brains thus far obtained from patients with kuru revealed widespread neuronal degeneration. The cerebellum and the extrapyramidal system were most severely affected. There were also changes in the anterior horn cells, inferior olives, thalamus, and pontine nuclei. Gross and microscopic pathological studies of other tissues from these 10 patients did not show any specific lesions. Acute meningoencephalitis with a mononuclear pleocytosis in the cerebrospinal fluid was discovered in the region, but it was impossible to establish any relationship between this infection and kuru. No antecedent encephalitic or meningoencephalitic illness or any other acute infectious disease was identified in the study of kuru, and no nutritional or toxic factor was incriminated as of possible causative significance in the disorder. A congenital familial tremor, which did not greatly interfere with a normal life in native society, was observed and was easily differentiated from the rapidly progressive degeneration in kuru. Genetic predisposition is strongly suggested, but any ethnic-environmental variables that are operating in the pathogenesis of kuru have not been determined.

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Excitomotor Syndrome Elicited by Drugs Exhibiting a Depressant Action on Neural Centers (Neuroleptics). J. Delay, P. Deniker, A. Green and M. Mordret. Presse méd. 65:1771-1774 (Nov. 2) 1957 (In French) [Paris].

Patients admitted to the clinic for mental and cerebral diseases in Paris were treated with reserpine, chlorpromazine, and proclorperazine, a new French chlorpromazine-like compound. Observations made on these patients confirmed previous reports by other workers that reserpine and chlorpromazine may cause reversible extrapyramidal symptoms. It is this effect which distinguishes reserpine and chlorpromazine from the classic sedatives and from certain other "tranquilizers," and it prompted the authors to suggest the term "neuroleptic" for these drugs.

In addition to bradykinetic and Parkinsonian manifestations which were frequently observed and which occasionally occurred unilaterally and with some delay after the administration of rather large doses of chlorpromazine and reserpine, other peculiar manifestations were particularly associated with proclorperazine. They were acute and transitory and occurred without delay after the administration of small doses of the drug. They were either of excitomotor type, such as tremor similar to that from a chill, myoclonia, sudden shaking with extension of the trunk, akathisia, and tasikinesia or of akinetic and occasionally of akineto-

hypertonic type with a fairly specific linguomasticatory and cervical localization, and they were associated with a condition of psychomotor hypersuggestibility, causing them to be considered as "hysteroid." Oculogyric crises similar to those which occur in patients with epidemic encephalitis were also noted. These observations provide supplementary data for explaining the neurophysiological mechanism of action of reserpine, chlorpromazine, and proclorperazine, and they also offer new therapeutic views. It seems possible that the excitomotor manifestations, which in addition to the extrapyramidal symptoms are elicited by these drugs, particularly those manifestations which are of crisis type, may yield therapeutic results which differ from the essentially sedative effects which up to now have been expected from these substances in the field of neuropsychiatry. Chlorpromazine should be given first a trial in patients with schizophrenia with catatonic excitement; reserpine or any other drug which may elicite excitomotor manifestations should be preferred in patients with schizophrenia with adynamia and apathy. The neuroleptic drugs seem to be least effective in endogenous melancholia and in the hypothymic forms of schizophrenia. They exerted a favorable effect on excitation, agitation, and impulses of patients with schizophrenia but also induced improvement of contact and apraxia.

GYNECOLOGY & OBSTETRICS

Regression of Human Metastatic Mammary Cancer Induced by 3-Methylcholanthrene. C. Huggins and J. D. McCarthy. Cancer Res. 17:1028-1032 (Nov.) 1957 [Chicago].

A solution of 3-methylcholanthrene in sesame oil (1 Gm. in 100 cc. of oil) was administered to 6 women between 49 and 63 years of age with mammary cancer. A dose of 20 mg. of the compound was administered intramuscularly daily to 3 patients. A daily dose of 50 mg. was given orally to 3 patients in whom exhausting nausea and vomiting occurred within 5 days, making withdrawal of the drug necessary. The patients receiving the drug intramuscularly complained at times of slight, transitory nausea, but it was mild and there was no great decrease of intake of food. In 2 patients a mild transitory diarrhea occurred. A gastric ulcer occurred in 1 patient during the administration of the drug, and 3-methylcholanthrene had no beneficial effect on the mammary cancer of this patient. The drug induced some regression of mammary cancer in the other 5 patients, 4 of whom have been treated earlier by adrenalectomy and oophorectomy. There was subjective and objective evidence of inhibition of the malignant process, and in 1 patient the regression was of major magnitude and had clinical therapeutic significance. This effect of 3-methylcholanthrene was remarkable, since the responding neoplasms were not dependent on hormones but were of undifferentiated types which have been hitherto refractory to inhibitory influences. In all the patients there were temporary decreases in the levels of circulating hemoglobin and serum proteins during the administration of 3-methylcholanthrene. These proteins increased in amount after the cessation of administration of the compound. It must be emphasized that the administration of 3-methylcholanthrene to human beings is potentially dangerous, since the compound may give rise to new neoplasms; but a carcinogenic effect was not observed in the patients in the brief period of 9 months.

Treatment and Prognosis in Cancer of the Ovary with a Review of a New Series of 143 Cases Treated in the Years 1944-1951. E. W. Munnell, H. W. Jacox and H. C. Taylor. Am. J. Obst. & Gynec. 74:1187-1200 (Dec.) 1957 [St. Louis].

In 1949, 2 of the authors published a report on the cases of cancer of the ovary treated at the Sloane Hospital during the period from 1922 to 1943. In this series there were 200 cases of primary cancer and 53 metastatic tumors of the ovary. The 5-year cure rate for the cases of primary cancer during this period was 27.5%. This was a relatively good figure, but it was admitted that the figure reported in any article was at least as dependent upon the pathological criteria for malignancy and the categories included as on any actual or claimed excellence of treatment. For the further study of this problem, the authors now report an additional 148 cases of primary cancer treated during the years 1944-1951, inclusive, for which 5-year end results are available. On the basis of these new cases, the authors reexamined the subject to determine whether any significant improvement in therapy has been accomplished. In comparing the 2 groups, the importance of histogenetic type, histological grade, and stage of clinical extension in prognosis has again been stressed. No significant improvement in the results in the more recent as compared with the earlier period was noted. The prospect of chemotherapy and of improved x-ray therapy is discussed.

PEDIATRICS

Combined Immunization Against Diphtheria and Whooping-Cough in Infants Aged 2-5 Months. G. Bousfield. Brit. M. J. 2:1216-1217 (Nov. 23) 1957 [London].

It has previously been observed that immunization against diphtheria and whooping cough would appear to be much safer with children 3 to 6 months of age than with the older age groups, owing to the relative infrequency of poliomyelitis during the first few months of life. All the sub-

jects studied in this report were in the 2-5 month age group, and all were given 3 monthly injections of 1 ml. of W. D. P. (diphtheria toxoid with pertussis vaccine). Schick tests were performed on these children at the age of 15 months. Of 1,641 cases, 941 were Schick positive and 700 Schick negative before immunization. After immunization, 938 (99.68%) of those who were Schick positive and 698 (99.71%) of those who were Schick negative were Schick negative, indicating that maternally bestowed antitoxin does not in any way interfere with the ultimate development of satisfactory immunity when a 3-dose course of W. D. P. is given at monthly intervals. The question of the satisfactory duration of this immunity up to school-age without intermediate booster immunizations beyond the slight stimulus of the Schick test performed at the age of 15 months is resolved with the testing of children who were inoculated with 3 injections of W. D. P. more than 4 years previously at the age of 2 to 5 months. In 148 children of this group, 91.9% of the 74 who were Schick positive before immunization became Schick negative, and 95.9% of the 74 who were Schick negative retained this state. Protection against severe or even moderate whooping cough was also shown to be of a high order.

The Roentgenographic Diagnosis of Geophagia (Dirt-Eating) in Children. J. E. Gardner and F. Tevetoglu. J. Pediat. 51:667-671 (Dec.) 1957 [St. Louis].

Sixty children, all proved dirt eaters, ranging in age from 11½ months to 4½ years and all residents of Nueces County, Texas, had anemia, achlorhydria, and dirt in the feces. All of the children, 53 (88%) of whom are Latin Americans, came from low-income family groups and had easy access to earth. X-ray was used as a primary as well as a secondary means of diagnosis, the diagnosis in the former group being incidental in patients coming to the clinic for complaints unrelated to geophagia. The diagnosis of geophagia in the second group, based on either a history arousing suspicion of dirt-eating or anemia, was confirmed by x-ray. An anteroposterior view of the abdomen was sufficient for the demonstration of dirt in the colon, although it is necessary to rule out the ingestion of any medicine or administration of heavy metals, such as barium or bismuth. Chest films are sufficient for diagnosis in patients with large amounts of ingested material in the colon where the appearance of dirt was fairly constant, varying only in the amount present. Two of the 4 cases on which semiquantitative spectrographic analysis was done did not reveal radiographic evidence of geophagia. Patients admitted to the hospital showed no dirt in the colon in 3 to 10 days, while patients treated at home showed dirt in the colon for 3 weeks, indicating that dirt-eating continued. One patient, so severely anemic that he was unable to walk, who had been treated to no avail with numerous vitamins, hematinics which included folic acid and vitamin B_{12}, and iron and liver preparations, responded to iron-cobalt mixture therapy; the response to the latter type of therapy was a consistent factor in all the cases in this series. All 60 patients exhibited hypochromic, microcytic anemia associated with achlorhydria, suggesting that in patients in whom the presence of an unexplained iron-resistant anemia or achlorhydria or a history that would lead one to suspect geophagia should be x-rayed to determine the presence or absence of dirt in the gastrointestinal tract.

Interstitial Plasma Cell Pneumonia and Pneumocystis Carinii. A. Ariztia, W. Bustamante, L. Moreno and others. J. Pediat. 51:639-645 (Dec.) 1957 [St. Louis].

In the past few years an increasing number of papers from European clinics have been published describing a severe respiratory disease which almost exclusively attacks premature and undernourished infants. The pathological findings show widespread interstitial infiltration of the lungs with mononuclear cells and plasmocytes and a peculiar foamy exudate in the alveoli. Most cases appear in an epidemic manner in the wards of childrens hospitals, and, although the etiology has not been definitely established, Vanek and Jirovec called attention to the presence in these cases of a parasite, Pneumocystis carinii, which is known to infect a wide variety of animals. Deamer and Zollinger published a review of this disease and stated that the disease entity seemed to be relatively unknown in the United States. Ariztia believed that the disease was found in Chile and that clinical diagnosis of it was made in several instances. Moreno studied special types of respiratory diseases which were diagnosed during life as bronchopneumonia and which occurred in premature and malnourished infants; these diseases were similar in all aspects to those described by the European pediatricians as interstitial plasma cell pneumonia, and the parasite Pneumocystis carinii was found in lung sections from these patients.

A clinical diagnosis of interstitial cell plasma pneumonia was made in 5 patients, the remaining 5 cases being diagnosed as bronchopneumonia. The onset of the disease occurred between 3 and 6 months postpartum in the 7 premature infants, in 2 infants born at term, and in 1 child whose birth weight was unknown. The clinical onset was characterized in 6 cases by increasing dyspnea, cyanosis, and anorexia, in 4 cases by rapidity, and in only 1 case by a persistently high fever. The clinical course of the disease was variable. In accordance with Torricelli's criteria, 7 patients were adjudged

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to have typical cases of interstitial plasma cell pneumonia, 2 to have disease similar to bronchopneumonia, and 1 to have a case of the asphyxia type with pneumothorax. The radiologic findings are so characteristic that, although they do not present a unique pattern, the constant association of the different findings make the radiologic picture almost pathognomonic. There is an extremely severe, persistent interstitial emphysema that flattens and immobilizes the diaphragm and causes, simultaneously, a protrusion of the aerated lung through the intercostal spaces and a mediastinal emphysema especially visible in the lateral position. The most constant factor is an emphysema that is present prior to the development of symptoms, is unrelated to the clinical picture, and persists after the symptoms have disappeared. The lack of physical signs associated with severe functional and systematic involvement and a high mortality rate further characterize a disease entity, for which a complement deviation test has been devised with use of an antigen extract of lungs of infants who have died of interstitial plasma cell pneumonia.

Palmar Pulsation: A Physical Sign of Patent Ductus Arteriosus in Infancy. D. Stuckey. M. J. Australia. 2:681-682 (Nov. 9) 1957 [Sydney, Australia].

In a child who fails to thrive or shows signs of congestive heart failure, the recognition of a patent ductus arteriosus becomes a practical problem because of the possibility of its surgical treatment. Often the murmur is not typical either in character or in site of maximum intensity, and reliance must be placed on the peripheral arterial signs. In a 2-month-old infant with characteristic signs of patent ductus arteriosus later confirmed by operation, it was observed that pulsation of the metacarpals could be easily felt in the palm of the hand as a strong, forcible pulsation. Subsequently, this physical sign was found in a number of children suffering from patent ductus arteriosus, and it was decided to try to assess its value from a diagnostic point of view. A group of children in whom the cardiovascular system was judged to be normal was examined for the presence of palmar pulsation. A group of children suffering from a variety of congenital heart defects other than patent ductus arteriosus was similarly examined.

On the basis of the results obtained in these studies the author arrives at the following conclusions: 1. In the absence of fever, severe anemia, and high environmental temperatures, palmar pulsation is rarely found in normal infants or in infants with various forms of congenital heart disease other than patent ductus arteriosus. 2. Palmar pulsation is usually present in children suffering from patent ductus arteriosus and is a useful confirmatory sign of the condition in infants. 3. Absence of palmar pulsation in a child under the age of 2 years makes it unlikely that a patent ductus arteriosus of any size is present.

OTOLARYNGOLOGY

Cramps of the Professional Voice. J. A. Pradillo. A. M. A. Arch. Otolaryng. 66:624-628 (Dec.) 1957 [Chicago].

Vocal cramps occur in such persons whose profession involves the use of the voice as singers, teachers, speakers, radio and television announcers, and jai-alai book makers. This last group consists usually of men with powerful baritone voices, although a few, to avoid fatigue, use af biphase or falsetto voice. Cramps may affect the extrinsic as well as the intrinsic muscles of the larynx and other muscles forming part of the vocal organs. The author gives special attention to the thyreoarytenoids, commonly called vocal cords. He describes the 2 types of muscular fibers found in these cords, pointing out that they resemble those of the myocardium from the point of view of their histological constitution as well as their physiology, since they have the property of fibrillating, of moving rhythmically, and of vibrating. Such muscles require a proportionally greater quantity of nutrients and especially oxygen to satisfy metabolic requirements than do other muscles. Vocal fatigue is a determining factor of the cramps, which occur after a prolonged period of vocal exercise. The cause is that in the muscular metabolism during the anaerobic phase the carbohydrates pass through various transformations—glycogen to glucose to glucose-6-phosphate to pyruvic acid to lactic acid—and an exaggerated muscular activity can promote the formation of an excessive quantity of pyruvic acid, thereby disturbing the succeeding phases of the metabolism. The incomplete combustion in turn creates a lack of oxygen (oxygen debt) necessary for the proper functioning of muscular fibers, especially when the activity is intense.

Apart from the main factor, which is fatigue, some special body conditions are necessary. Metabolic changes brought about by hormonal diseases and by those of general character, disturbances of glucide metabolism, and uricemia all have a bearing in the production of cramps. Pain develops, generally on the sides of the larynx, making it impossible for the person to emit any sound. It rarely lasts over 1 minute. The patients, trying massage as a corrective, may be able to go on singing, although the cramp may return immediately or after a few days. Cramps may return sporadically. The author differentiates cramps of the professional voice from other phonetic impediments such as "trac," neurovasomotor monochorditis, and "coup de fouet." The author comments on the histories of 9 patients with vocal cramps; by interviewing many

persons who use their voices professionally, he gained the impression that this type of cramp is comparatively frequent, especially when the person affected is beyond the age of 40, and that patients who experience it also frequently have cramps in other muscles of the body.

Continuing Clinical Study of Local Treatment of Allergic Rhinitis: Use of a Nasal Spray Containing Prednisolone Acetate and Chlorprophenpyridamine Gluconate. W. H. Evans. Ann. Otol. Rhin. & Laryng. 66:716-728 (Sept.) 1957 [St. Louis].

Considerable clinical and experimental evidence has accrued to furnish a firmer rationale for the topical use of corticosteroids in treatment of allergic inflammations in the nose. The prednisolone–chlorprophenpyridamine nasal spray was used in the majority of cases of allergic rhinitis as adjuvant therapy. Many of the patients have been followed for many years and have had various types of treatment, including systemic and topical antihistaminics of various types, specific desensitization, and antibiotics. Many had previously received treatment with the earlier preparation of cortisone and Chlor-Trimeton in the form of nose drops or nasal packs. During the past 15 months, in almost all patients with nasal allergy requiring continued symptomatic treatment, the cortisone–Chlor-Trimeton solution has been replaced by the prednisolone–Chlor-Trimeton suspension in a plastic spray bottle. The spray emitted is fine enough to reach all parts of the nasal lining, and it has the practical advantage of being much easier for the patient to use. The small bottle can be carried in the pocket or purse and used conveniently whenever symptoms require. Eighty patients have used the prednisolone–Chlor-Trimeton nasal spray, 37 the prednisolone preparation with phenylephrine added, and 21 with added phenylephrine and neomycin. Eleven in the second group and 2 in the last group also were among the 80 who received the basic preparation containing only prednisolone and Chlor-Trimeton.

The total number of patients, with sufficient follow-up for evaluation, was 125. Among these 125 patients who used the prednisolone nasal suspensions, 115 obtained significant relief. Observations on these patients and reports of other observers cited by the author furnish convincing proof of the efficacy of the corticosteroids and their analogues when applied topically to inflamed nasal mucosa in allergic conditions. Since prednisolone, generally speaking, appears to be safer and more effective than hydrocortisone (or as effective), it would appear, at present, to be the preparation of choice for this purpose. In practically all cases, the results obtained with the prednisolone–Chlor-Trimeton suspension parallel those observed with the older cortisone and hydrocortisone preparations, although an occasional patient claims to experience greater relief with one or another preparation.

Prevention of Adverse Effects of Streptomycin on the Ear. T. Ozaki. A. M. A. Arch. Otolaryng. 66: 673-678 (Dec.) 1957 [Chicago].

The author reports on adverse after-effects observed in 39 patients who had been referred to the otorhinolaryngological department from the tuberculosis department as suspected of having untoward effects of streptomycin; 29 of the patients were observed for a certain period. Two or more audiograms had been taken in these patients, the first before the onset of treatment and the others at intervals of 10 days after the onset of treatment. These patients had received intramuscular injections of 1 Gm. of streptomycin twice a week. Adverse effects resulting in impairment of hearing was observed in 10 of the patients after they had received only from 2 to 10 Gm. This suggests that the amount of the drug is not necessarily the decisive factor in streptomycin intoxication but that individual sensitivity also plays a part. If streptomycin exerts adverse effects on hearing, the audigram shows reduced perception of high-pitch sound and gradually that of low-pitch sound. If the audigram shows any change, the author recommends that 100 mg. of fortified vitamin B_1 be administered intravenously daily. During this treatment, audiograms are taken every 10 days. If they show improvement, this treatment should be continued until there is complete recovery. To prevent recurrence, the treatment should be continued as follows: the first month twice a week, the second month once a week, and the third month 2 or 3 times monthly. This treatment should cover a 6-month period, and the number of treatments should be gradually reduced. On the other hand, the administration of streptomycin should be discontinued and some other antituberculosis drug given.

The intravenous administration of fortified vitamin B_1 produced favorable results in 15 patients. Early detection is possible when impairment of hearing is preceded by abnormal changes in the audiogram. Early treatment is recommended, because advanced impairment is difficult to cure. Early symptoms are slight otalgia, feeling of obstruction of the ear, consciousness of compression of the ear, and tinnitus without difficult hearing. As prophylaxis, intravenous administration of 100 mg. of fortified vitamin B_1 is suggested immediately before or after administration of streptomycin (dihydrostreptomycin or combined streptomycin), with repetition the following day. Since the introduction of this method of prophylaxis, there has been a steady decrease in the number of patients with impaired hearing from the tuberculosis department.

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THERAPEUTICS

Clinical Implications of Isoniazid Blood Levels in Pulmonary Tuberculosis. R. S. Mitchell and J. C. Bell. New England J. Med. 257:1066-1070 (Nov. 28) 1957 [Boston].

Isoniazid hydrazones, acetylated isoniazid, isonicotinic acid, and isonicotinic acid conjugates, in addition to free unmetabolized isoniazid, have been found in the urine of human subjects given a single oral test dose of isoniazid. This metabolic alteration is so extensive that as little as 1% of a test dose may be exreted in the urine free and unaltered and as much as 60% of a dose may be excreted in the acetylated form. Only the free drug, however, possesses significant antimicrobial activity against tubercle bacilli. The other metabolites, at least in the concentrations encountered, have no antimicrobial activity. In view of the urinary-excretion findings, it has been assumed that the inactive isoniazid present in serum is mainly the acetylated derivative. Isoniazid acetylation is accomplished by the same enzyme system that is involved in the acetylation of aminosalicylic acid, para-aminobenzoic acid, sulfonamides, and other compounds. Any 2 of these compounds in mixture will compete with each other for the acetylating process. It was found that aminosalicylic acid given with isoniazid to human subjects was frequently followed by a rise in serum concentrations of biologically active isoniazid.

A small number of patients continue to expectorate tubercle bacilli that are sensitive to streptomycin, isoniazid, and aminosalicylic acid in spite of prolonged treatment with these drugs. Presumably, such patients metabolize isoniazid so extensively that inadequate amounts of free drug exist in body fluids. A good correlation was found between the amount of free isoniazid excreted in the urine and the development of isoniazid neuritis. The implication was that persons who do not metabolize isoniazid extensively and who thus excrete large amounts of free drug in the urine probably have higher concentrations of free, biologically active drug in the serum and hence have a greater chance of toxic reactions to isoniazid.

To ascertain whether these observations have significant clinical implications, the authors made studies on 226 persons of whom 208 had active tuberculosis. They found that serum levels of biologically active isoniazid show some correlation with the bacteriologic response to isoniazid. With the use of a single test dose of 4 mg. of isoniazid per kilogram of body weight, it is tentatively recommended that the dosage be adjusted so as to achieve serum isoniazid bioassay levels of at least 3.2 mcg. per milliliter at 2 hours and 0.8 mcg. at 6 hours. One-third of the daily ration of aminosalicylic acid should be added to the test dose if it is to be used in actual therapy. Seven patients were found who continued to excrete tubercle bacilli susceptible to isoniazid after 6 months or more of chemotherapy including that drug. Serum bioassay levels in 5 of these 7 patients were quite low in comparison to those in most but not all of 41 similar patients exhibiting isoniazid resistance. The rate of isoniazid inactivation as measured by the bioassay technique does not appear to be influenced in adults by age, sex, character, or extent of tuberculosis or by other diseases, such as cirrhosis, diabetes, renal insufficiency, silicosis, and diffuse pulmonary emphysema.

Trichomonas Vaginitis: Clinical Trial of a Mixture of an Antiseptic With Local Anaesthetics. H. C. Stewart, W. H. Hughes, E. G. Thomas and W. C. Nixon. Lancet 2:1028-1030 (Nov. 23) 1957 [London].

In the treatment of trichomonas vaginitis, the efficiency of an antiseptic preparation containing benzalkonium chloride, amethocaine, and amylocaine (Locan) was compared with that of naphthylmethane disulphonate (Penotrane) and Acetarsol, which is a British preparation of 3-Acetamido-4-hydroxybenzenearsonic acid (Acetarsone). Primary manifestations were controlled in all cases with Locan, although 34 and 32% of the cases did not respond to treatment with Penotrane and Acetarsol respectively. Only 16% of the patients controlled with Locan required more than 1 week of treatment, occasional patients requiring up to 4 weeks treatment with increased dosages before control was obtained. Reinfestation was equally common with Acetarsol and with Locan and was even more common with Penotrane. Reinfestations were controlled with Locan with the same expediency as the initial infection, and resistant strains were not found; however, the preparation (Locan) is capable of being modified to meet the threat of resistance forming organisms. It seems reasonably certain that Locan will control the individual infestation with trichomonas, but neither this nor any other preparation can be expected to prevent reinfestation once treatment has been stopped, nor is it likely that treatment of the female alone will eradicate the organism from the community and prevent reinfestation; a period of 3 months is deemed necessary for a male carrier state to die out.

Treatment of Juvenile Thyrotoxicosis with Potassium Perchlorate. J. M. Smellie. Lancet 2:1035-1036 (Nov. 23) 1957 [London].

Since hyperthyroidism in children is rare (1-2½% of all cases), experience in its therapy is limited and the merits and demerits of various therapeutic procedures are controversial. The ultimate outcome of the removal of some part of the gland is speculative. To remove too much is catastrophic, and to remove too little necessitates reoperation.

McClintock and others report that, of 45 children who underwent subtotal thyroidectomy, 13 showed hyperthyroidism afterwards, 4 had clinical evidence of hypocalcemia presumably due to hypoparathyroidism, and, of 22 children with bilateral exophthalmos prior to operation, 6 failed to show improvement. Treatment by external irradiation or by radioactive iodine is unsuitable for children because of the possible sequelae. Thiouracil and its compounds are effective against thyrotoxicosis, but they are capable of producing dangerous toxic reactions, such as agranulocytosis, drug fever, and rashes.

Stanbury and Wyngaarden showed that potassium perchlorate can displace iodine from its position in the thyroid gland. No toxic effects other than mild gastrointestinal upset were observed in 24 patients with hyperthyroidism effectively controlled by the administration of 200 to 400 mg. of potassium perchlorate by mouth every 8 hours. Graves disease in a group of 108 patients was effectively controlled over a 10-month period with potassium perchlorate. The case reports of 6 children would seem to substantiate the role of potassium perchlorate in the treatment of juvenile thyrotoxicosis. No untoward side-reactions other than gastrointestinal upset or hypothyroidism have been observed in children in a period of treatment of as long as 3 years. Whether potassium perchlorate can restore all children with hyperthyroidism to health and thus render surgery unnecessary has yet to be ascertained. The experience gained to date suggests that treatment will be required for a period of up to 3 years and perhaps through puberty. Should this drug keep a child euthyroid through puberty, it will delay thyroidectomy to the time when the procedure would be comparatively safer and of greater value. Two additional points are deserving of mention: (1) a patient whose thyrotoxicosis is controlled with perchlorate would be liable to have a relapse if his blood-iodide level was suddenly raised, and (2) the cost of treating the first patient in this series continuously for a period of 3 years was approximately $1.00.

Action of Gamma Globulins in Treatment of Infections. A. Ravina. Presse méd. 65:1776-1778 (Nov. 2) 1957 (In French) [Paris].

A preview of the literature on the use of gamma globulins for the treatment of infections showed that the combination of gamma globulins with antibiotics, particularly with chloramphenicol, proved extremely effective in the treatment of experimental infections in mice, while the same doses of gamma globulin or antibiotic when used separately were incapable of controlling the development of these infections. Clinically, similar therapeutic results were obtained. The curative action of gamma globulins when used alone has not been clearly defined yet, but certain observations suggest that patients with infections refractory to antibiotic therapy were benefited by gamma globulin therapy, provided that the gamma globulin used was obtained from blood which contained antibodies which protect against the disease to be treated, particularly against those caused by streptococci, micrococci (staphylococci), pneumococci, and the viruses of measles, hepatitis, and poliomyelitis, but not against those caused by Salmonella strains. The gamma globulins exert their action only on those pathogenic agents which are present in the extracellular spaces. Nevertheless, the gamma globulins exert a notable neutralization effect on the bacterial toxins, and that represents an advantage when compared with the antibiotics which are bactericidal or bacteriostatic agents. These findings are suggestive, although the mechanism of the synergistic action of gamma globulins and antibiotics has not been completely elucidated.

The Treatment of Acute Porphyria with Chelating Agents: A Report of 21 Cases. H. A. Peters, S. Woods, P. L. Eichman and H. H. Reese. Ann. Int. Med. 47:889-899 (Nov.) 1957 [Lancaster, Pa.].

Twenty-one patients between the ages of 22 to 55 years with a ratio of 2:1 of women to men, 20 of whom had acute intermittent hepatic porphyria and 1 of whom had mixed hepatic porphyria, were treated with 2, 3-dimercaptopropanol (BAL) and disodium calcium ethylene diamine tetraacetate (EDTA). BAL was used in a 10% solution in 20% benzyl benzoate in peanut oil. Doses ranged from 50 to 1,200 mg. per 24 hours in divided doses, given for 4 to 60 days consecutively. Several patients received 1-3 injections of 100 to 300 mg. weekly for as long as 2 years. Eleven patients received BAL alone. Administration of BAL was combined with intravenous administration of EDTA in 6 patients, who were given 1-10 Gm. of EDTA in a 24-hour period, diluted in 5% dextrose in water in a ratio of 2.5:5 Gm. of EDTA per 1,000 cc. The drug was given usually over 2 to 4 hours for 2 to 5 consecutive days. EDTA in tablets of 0.5 Gm. was occasionally given usually over 2 to 4 hours for 2 to 5 consecutive subacute phases of the disease.

Multiple signs and symptoms were observed in the patients before therapy was started. Eight patients had bulbar symptoms in the form of dysphagia, diplopia, anisocoria, and facial and/or laryngeal palsies. Three patients had Jacksonian seizures, and 7 had convulsions of the grand mal type. Thirteen patients had excited catatonic, schizophrenic-like psychosis and hysterical and depressive reactions. Eight patients had peripheral neuropathy. Constipation was noted in 12 patients. Two patients had temporary oliguria and another urinary retention. The burgundy or brownish urine commonly described in textbooks was seldom mentioned by the patient. A malar flush, diffuse dusky complexion, and hirsutism were noted. Thirteen of

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the 20 patients with acute intermittent porphyria and the patient with mixed porphyria were improved by the effect of chelation. BAL and EDTA were both effective, although in the dosage employed BAL occasionally seemed to act more rapidly.

Four patients responded equivocally to chelation therapy; in 2 there was no change, and 1 patient with periarteritis and porphyria died. Chelation may be effective after failure of corticotropin (ACTH) therapy and vice versa. Two patients received hydrocortisone several days during chelation therapy because of oliguria, and diuresis promptly followed. Heroic nursing and supportive care, including tracheotomy, are essential in severe cases; all patients must avoid exposure to barbiturates, sulfonamides, heavy metals, oil paints, and solvents. Pronounced chlorpromazine (Thorazine) sensitivity was noted in 1 patient with neuropsychiatric symptoms. Elevation of zinc-urine excretion was noted during acute episodes preceding chelation and paralleled the symptoms more closely than abnormal porphyrin excretion. An acceptable explanation for the effectiveness of chelation in porphyria remains uncertain. The ultimate answer may be found in an increased understanding of metallo-enzyme systems.

Use of a "Double-Blind" Study Investigating the Clinical Merits of a New Tranquilizing Agent. H. Koteen. Ann. Int. Med. 47:978-989 (Nov.) 1957 [Lancaster, Pa.].

Thirty-seven bottles, each containing 50 capsules of a propanediol derivative known as 2-methyl-2-n-propyl-1,3 propanediol dicarbonate (Miltown) and 36 bottles of a placebo were distributed to 25 patients who manifested anxiety, muscle tension, restlessness, and irritability. Each patient acted as his own control. The period evaluated consisted of about 1,000 patient days. During the first portion of the experiment the patients were urged to take 3 capsules daily, each capsule containing 400 mg. of the agent. This is the same amount as is currently distributed in the commercially available Miltown; it is identical to Equanil, which is marketed under a different trade name but is chemically the same. Both products are referred to as "tranquilizing agents." Subsequently, patients were urged to take 4 capsules daily, and this was the average dose maintained for most patients, but in some instances as much as 4,800 mg. were taken daily. When a patient returned with an enthusiastic report he was given, without comment, another bottle of medication which appeared indistinguishable to both patient and physician. If the patient expressed the belief that he had not benefited from the previous medication, he was then given another numbered bottle with the suggestion that this contained more of the therapeutic agent. The significant aspect of this technique was that it allowed the patient the privilege of being critical of the medication and not of the physician, because he understood that he would be given a more effective capsule on his next visit.

Results revealed that Miltown in the recommended dosage of 1,200 to 1,600 mg. daily had no greater effect in relieving symptoms than did the placebo in this group of unselected patients. The effects of larger doses on the central nervous system were not explored. It appears that the tranquilizing agent that has been used longest, most frequently, and most effectively is still the placebo. The patient is influenced by the dynamic association with the physician and gains a sense of security from a visit with a compassionate person; the response is directly proportionate to his need for emotional support. A very significant problem that has resulted from the use of the so-called tranquilizing agents is that they also "tranquilize" the physician. The possible harmful effect of this is immediately apparent when it is considered that structural disease processes may be overlooked and also that the physician assumes less responsibility for understanding and helping the patient.

Oral Treatment of Diabetes Mellitus with 1-Butyl-3-p-Tolylsulfonylurea (Compound D 860). G. Angeli. Minerva med. 48:2772-2785 (Sept. 1) 1957 (In Italian) [Turin, Italy].

Tolbutamide (Compound D 860), whose chemical formula is 1-butyl-3-p-tolylsulfonylurea, was given orally to 60 patients with diabetes mellitus, of whom 40 had not previously received oral medication for diabetes mellitus and of whom 20 had previously received Carbutamide (Compound BZ 55). Determinations of daily blood and urine sugar levels and azotemia were carried out before and during the treatment. The dose of tolbutamide on the first day was 2.5 Gm., given to the patients in the fasting state in the morning. The dosage was gradually decreased on the subsequent days until a maintenance dose was established. The patients received the drug twice a day after the noon and evening meals.

Marked decrease in blood and urine sugar levels was observed in some patients within a few days, while in others this occurred later, sometimes after a month. Positive results were observed in 52 patients and negative in 8. A positive result was considered when it was possible to substitute tolbutamide therapy partially or entirely for insulin therapy. Failure to substitute tolbutamide for insulin therapy or worsening of the status were interpreted as negative results. Best results were obtained in patients who had previously received a small dosage of insulin or no insulin. Few unfavorable effects were observed, and these affected only few patients. These included slight headache, disturbed digestion, and blurred vision. In the course of prolonged tolbutamide therapy it was

necessary to increase the dosage in some patients in order to maintain the initial effect of the drug. Tolbutamide did not cause a sudden decrease of blood sugar level, thus enabling the anticipation of hypoglycemia. Hypoglycemia occurred in some patients with the mild status. To obtain the same effect with tolbutamide as with carbutamide therapy, a larger dosage of tolbutamide was required for patients in whom tolbutamide therapy was substituted for carbutamide therapy; tolbutamide was better tolerated. Reinstitution of insulin therapy after withdrawal of tolbutamide therapy apparently produced better therapeutic results than an exclusive insulin therapy. A combination of tolbutamide and insulin seemed to bring under control certain types of diabetes which were difficult to manage with insulin therapy alone. Tolbutamide medication also caused an improvement in patients who had diabetes associated with hemochromatosis.

RADIOLOGY

The Roentgenographic Findings Associated With Neuroblastoma. C. F. Hansman and B. R. Girdany. J. Pediat. 51:621-633 (Dec.) 1957 [St. Louis].

Neuroblastoma is a malignant tumor which metastasizes to the bony and nonbony structures. Observations on 30 children, 16 boys and 14 girls ranging in age from 1 month to 10 years, in each of whom the diagnosis of neuroblastoma or ganglioneuroblastoma was confirmed histologically, revealed palpable abdominal masses in 24 instances. The site of the primary tumor was found to be the adrenal gland in 14 instances; the site of the primary tumor was retroperitoneal in 5 and was unknown in 7 patients. Fever was the chief symptom in 12 children, 9 complained of pain in the legs, 8 were anoretic, and 7 were tired and listless. All patients had x-ray films of the abdomen, urinary tract, and skeleton. An intra-abdominal soft tissue mass was visualized in 26 patients; in 25 of these it displaced adjacent structures. Bony or soft tissue changes of metastatic neuroblastoma were seen in 11 children. In 3 patients the bones alone were affected, in 2 the changes were limited to the lungs and meninges, and in 6 children there were combined bony and soft tissue metastases, pulmonary metastases being present in 4 of the latter group. Seven children had metastatic lesions in the skull, including 4 children with roentgenographic signs of increased intracranial pressure; 8 children had lesions in the femur, and 4 showed changes in the bony pelvis.

Another roentgenographic indication of soft tissue involvement is widening of the cranial sutures due to masses of tumor tissue between the dura and the calvarium so that a roentgenogram showing widened sutures and destruction of the bones of the cranial vault is pathognomonic of metastatic neuroblastoma. Bony metastases occurred most frequently in the skull and the femurs. The bones of the lower and upper extremities were late involvements, and the bones of the hands and feet were not affected. The palpable abdominal mass is of itself rarely diagnostic. The differential diagnosis must consider neuroblastoma. Wilm's tumor, hydronephrosis, polycystic kidney, lymphosarcoma, mesenteric cyst, and renal vein thrombosis. Preoperative differential diagnosis between neuroblastoma and Wilm's tumor may not be possible, may not even be made at surgery, and generally awaits histological proof. When the tumor has metastasized and leg or back pain is the presenting symptom, leukemia, scurvy, tuberculosis of the spine, osteomyelitis, acute rheumatic fever, and poliomyelitis must be ruled out. The skeletal changes of leukemia and metastatic neuroblastoma are radiographically indistinguishable, in which instance bone marrow aspiration is useful in establishing a diagnosis which otherwise awaits microscopic examination of surgical specimens. Bone marrow smears were positive in 4 children in whom there were no abnormal radiographic changes in their bones.

Roentgenologic Diagnosis and Differential Diagnosis of Regional Enteritis. H. G. Schmitz-Dräger and P. Thurn. Fortschr. Geb. Röntgenstrahlen 87: 566-574 (Nov.) 1957 (In German) [Stuttgart, Germany].

When regional ileitis was first described as a separate entity, it was identified as a chronic nonspecific inflammation of the terminal ileum with characteristic histological changes. Later, when it was realized that other sections of the intestine could become involved, the concept of regional enteritis evolved. The roentgenologic aspects of the various phases of the disease are demonstrated on the basis of the histories of 4 patients, and the underlying pathological lesions are discussed. The roentgenologic changes are (1) changes in the wall of the intestine, consisting of thickening, rigidity, separation of loops and stenosis; (2) changes in the intestinal mucosa as shown in coarsening of loops, polypoid or reticular relief patterns, or loss of a distinct relief pattern with stenosis; and (3) secondary changes such as adhesions, internal and external fistulas and abscess formation. In 1 patient the duodenum, jejunum, and ileocecum were involved. The roentgenologic differential diagnosis of regional enteritis must consider tumors in addition to chronic intestinal inflammations. If the lesion is localized in the terminal ileum, it may prove difficult to differentiate it from intestinal tuberculosis or from ulcerating colitis.

BOOK REVIEWS

The Biologic Basis of Cancer Management. By Freddy Homburger, M.D., Research Professor of Medicine, Tufts University School of Medicine, Boston. Forewords by Lauren V. Ackerman, M.D., Clarence Cook Little, Sc.D., and Alton Ochsner, M.D. Cloth. $10. Pp. 354, with illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1957.

This text is divided into four parts, dealing with the cause, biological behavior, diagnosis, and treatment and prevention of cancer respectively. The author presents recent advances in biology, experimental pathology, biochemistry, cytochemistry, and physics, as well as a framework of reference of a more historical nature. The relationship of the studies that have been made in these disciplines is then correlated with the clinical problems of the individual patient. There has long been a need for such a book, and one of the most frequent requests of medical students is for such a range of material in concise and understandable form. Although the author has attempted to describe the various aspects of cancer under one cover in a fashion that has not previously been attempted, he has fallen short of his goal. The principal reason for this is found in the preface, wherein the author states that the book was rejected by one publisher because eminent consultants believed "that no one person could write such a book." A more precise and accurate text could surely have been produced by a number of contributors representing various disciplines.

In the chapter dealing with characteristics and clinical course of human cancer, there is little attempt to explain the natural history and response or lack of response to treatment in terms of biological characteristics. Nine figures are used to portray the duration of life in untreated cancers in as many sites, with the remark, "Cancer of the breast is the least malignant of the neoplasms studied, because about 20% of untreated patients were still alive five years after onset of symptoms." There is no suggestion that carcinoma of the uterine cervix or of the larynx, for example, have a far more favorable biology and response to treatment than is the case for carcinoma of the breast. Carcinoma of the nasopharynx is described as "the most frequently overlooked site of curable neoplasms," while carcinomas of the hypopharynx are referred to as having a most insidious clinical evolution, with metastases being present in most patients when they are first seen. The fact is that these two sites are both biologically unfavorable, and, if anything, the hypopharynx presents a somewhat more hopeful problem. No mention is made of the fact that in men cancer of the lung now exceeds gastric carcinoma in frequency. It is highly misleading to state, as the author does, that x-ray examination leads to discovery of all cancers of the rectosigmoid. The author states that a large percentage of patients with carcinoma of the corpus uteri have metastases when first seen and gives as one reason that the symptom of vaginal bleeding is "inconspicuous." Inasmuch as most endometrial carcinomas occur in the postmenopausal era, vaginal bleeding is a conspicuous and often alarming signal to most women, and most of these lesions are still localized to the uterus when first seen, with 5-year control rates of about 70% rather than the less optimistic estimate quoted.

The discussion of the principles of surgery in cancer also neglects any real biological considerations. Pneumonectomy rather than lobectomy for carcinoma of the lung is strongly recommended, and the author is apparently unaware of the increasing use of lobectomy for favorable lesions and the relatively favorable results in lesions suitable for lobectomy as compared to pneumonectomy. The chapter on principles of radiotherapy is excellent, with a concise description of radiation physics, radiobiology, and clinical radiology, but in a discussion of dosage, no reference is made to the commonly accepted description of the quality of a beam of irradiation in terms of its half-value layer. For the clinician, there is much valuable information concerning the chemistry of carcinogens and the biochemistry of hormones. Even here there are some inaccuracies. On page 93, the representation of estrone fails to show the five-membered ring; on page 112, testosterone and cis-testosterone are depicted as different substances, whereas they are the same according to the newer nomenclature and what is meant is probably testosterone 17 alpha. On page 135, delta-9-3-iso-androstene-3-alpha-ol-17-one should be delta-9(11)-5-isoandrostene-3-alpha-ol-17-one. This book should be of most value to medical students for the reasons outlined above. It should also be of value to nonmedical research workers, particularly those new to the field of cancer research. The format of the book is admirable. A valuable list of references is keyed into each section of the book.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

The Century of the Surgeon. By Jürgen Thorwald. Cloth. $5.95. Pp. 432, with 66 illustrations. Pantheon Books, Inc., 333 Sixth Ave., New York 14, 1957.

This well-documented work on surgical history should have as much appeal for the interested lay reader as for the surgeon. By making the narrator an actual eye-witness of nearly all of the more significant events that marked surgical progress in the 19th century, the author has given his narrative much of the interest and excitement of a good novel. His spokesman is a young doctor, with friends and acquaintances in the profession both here and abroad, who grows with the profession until at the end of the book he has seen and participated in the epochal achievements that took place in his lifetime. He was personally acquainted with such giants of surgical growth as Semmelweis, Koch, Lister, and Harvey. Of those whom he did not actually meet he had what amounted to an intimate knowledge through acquaintances they had in common. His descriptions of operations performed without benefit of anesthesia are realistic and not likely to be forgotten by anyone who reads them. He is eloquent on the subject of the unsanitary practices that were taken for granted in the world's hospitals before Semmelweis awakened the medical and surgical world at the cost of his sanity. He saw and shared the "first beginnings" of use of sterilization, antisepsis, anesthesia, roentgen rays, prophylactics, and countless instruments. He was present when Morton gave the first anesthetic to a surgical patient. By a series of coincidences, he arrived at various points in the world just in time to witness many great surgical events. There is a convincing sense of immediacy about the story, and this is heightened at times by flashbacks revealing the conditions prevailing before the discoveries were made.

Since the emphasis throughout is on the more sensational and compelling events of the century from the surgeon's point of view, many lesser advances are omitted and those included are familiar to surgeons and others who have read much medical and surgical history. Even such readers as these, however, cannot fail to be interested, if only because of the novel approach. For readers more or less unfamiliar with the subject, the story as told should be not only informative but exciting.

The Closed Treatment of Common Fractures. By John Charnley, B.Sc., M.B., F.R.C.S., Orthopaedic Surgeon, Manchester Royal Infirmary, Manchester. Second edition. Cloth. $10. Pp. 260, with 199 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1957.

This well-written and adequately illustrated book shows thoroughness in both writing and investigation of the author. However, there are many sections of the book that express the author's opinion quite dogmatically.

This book is timely, stressing the closed treatment of fractures in contrast to the definite tendency at present to do open reductions with the insertion of considerable "hardware." The author does agree that there are many instances in which open reduction is the method of choice. The chapter on plaster technique is well worth reading, although it, too, contains several controversial points. Most will agree, however, that a sufficiently slow-setting plaster should be employed to allow the surgeon sufficient time to mold the cast well and to obtain the three-point pressure immobilization that is so necessary for a good result. This book is recommended as a reference book for the younger orthopedist and is valuable for all to read so that a better evaluation of closed versus open methods of treatment may be made.

Bone Diseases in Medical Practice By I. Snapper, M.D., Director of Medicine and Medical Education, Beth-El Hospital, Brooklyn. Cloth. $15. Pp. 229, with 48 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1957.

This well-written book deserves high praise. The first chapter deals with the physiology of bones. Most of the book deals with specific bone changes. Each chapter is practically a monograph and ends with an excellent list of references. The author raises the question as to whether the gravure process for the reproduction of roentgenograms is worth the extra work it has entailed. Those reproduced here, some of the finest ever published, would appear to indicate that they are. The only criticism might be that it would be easier to follow the text if the roentgenographic reproductions were placed in the chapter where they are discussed rather than at the back of the book, but this might have added too greatly to the cost. This book is recommended as a reference work to all who are interested in bone diseases.

Introduction to Urology. By Frank C. Hamm, M.D., M.S., F.A.C.S., and Sidney R. Weinberg, M.D., F.A.C.S. Elizabeth Cuzzort, medical illustrator [and] production director. Paper, loose-leaf. Pp. 293, with 259 illustrations. Research Foundation of State University of New York, 451 Clarkson Ave., Brooklyn 3, [n. d.].

In this comprehensive textbook urological diseases are well described with the aid of adequate and appropriate radiologic and pathological illustrations. The presented concepts of therapy are current, and controversial subjects are largely avoided. The binder type of format makes possible page changes necessary to keep the subject matter current. The bibliography is extensive. This type of textbook is ideal for student use and for ready reference for practitioners encountering urological problems.

QUESTIONS AND ANSWERS

EXPIRATION DATE OF POLIOMYELITIS VACCINE

To the Editor:—*Is poliomyelitis vaccine still potent enough to use one or two months after the expiration date if this vaccine has been kept under proper refrigeration?*

M. D. Hornedo, M.D., El Paso, Texas.

Answer.—The expiration date of poliomyelitis vaccine has been established at six months following the date of shipment from the manufacturer. The current regulations also permit a maximum of six months storage by the manufacturer prior to shipment. This expiration time has been selected on the basis of the best data available concerning the decay of antigenic potency of stored vaccine. Variations in this time-decay curve have been encountered between different batches of commercial vaccine. Thus, in many lots of vaccine there may be little or no loss of potency in six months, while other lots may decline in potency during storage. This decay is gradual, and of course the vaccine does not deteriorate to the degree that potency is greatly reduced at expiration. However, for poliomyelitis vaccine as for other biologicals, it has been necessary to designate an exact expiration date, and the interval has been selected such that a considerable "margin of safety" is maintained. At the present time no new evidence has appeared which would permit any extension of this expiration date. Until such time as further data or improved manufacturing techniques allow extension of the expiration interval, the use of outdated vaccine cannot be recommended.

TREATMENT OF SAND FLEA INFESTATION

To the Editor:—*What local treatment can be used for infestation of the scalp, pubis, extremities, and axillae by the Tunga penetrans, or sand flea? Local removal, especially from the scalp, by instrumentation is not feasible because of the extensive involvement.*

M.D., New York.

Answer.—Insecticides such as a 25% emulsion of benzyl benzoate or an ointment containing 1% gamma benzene hexachloride can be applied locally to kill the parasites. However, unless the bodies of the insects are removed, they will act as a continuing source of irritation until they slough out. There is no better way of removing the parasites than by means of a needle or other pointed instrument or a fine forceps. The opening of the "burrow" in which the body of the insect is lodged may need to be enlarged in the process. Subsequent local treatment would depend on the character and degree of the inflammatory response. Gentle but thorough cleansing followed, perhaps, by wet dressings with dilute Burow's solution should be helpful. An antibiotic ointment locally or, perhaps, systemic antibiotic medication may be needed to control secondary bacterial infection.

STERILE GLOVES AND MINOR SURGERY

To the Editor:—*Is it all right to do minor office surgery without the use of rubber gloves? A large clinic in one of the mainland cities does not use gloves in any of its clinical work, which includes minor surgery. The physician can scrub his hands and then use a known effective germicide; another method, which shortens the time of scrubbing preparation, is to scrub with sudsing emollient with 3% hexachlorophene. Why is not this equal or superior to the wearing of gloves when one does not know always if the gloves have been contaminated in some way? If you prepare the hands thoroughly you know that they are sterile. I understand that rubber gloves are not now in use in major surgery in Japan. Joseph Price of Philadelphia, who established a large hospital there some years ago and wrote a book on major surgery, had abandoned the use of rubber gloves and maintained in his book that one could sterilize the hands well and also could do surgery much better, as the tactile sense is much better without the use of gloves.*

Taber A. Darling, M.D., Agana, Guam.

Answer.—It is perfectly true that certain clinics have discarded the use of gloves and that during the war some of the foreign countries could not get rubber gloves, being forced, therefore, to operate bare-handed. In one large clinic in North America, even vaginal examinations are done without gloves. However, such usages are not standard practice, and if a patient sued because of a wound infection and the physician had not worn gloves although they were available, he might have difficulty in proving that due precautions had been taken and that the usual practices had been employed.

No patient ever has "sterile" skin and no physician ever has "sterile" hands, no matter how long he scrubs nor with what highly touted solutions.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

Wound infection develops because there are more bacteria present than the tissues can cope with, and the desired result is to have as little contamination as possible. When minor surgery is done in the office a clean excision of lipoma may follow drainage of an infected sebaceous cyst, and it certainly is better to change gloves than to depend on scrubbing between cases and not using gloves. Furthermore, scrubbing, no matter with what agent, gives only a clean surface skin and affects little if at all the various hair follicles, sweat glands, oil glands or even deep creases and folds. The hands are the cleanest immediately after scrubbing and become progressively more "dirty" with gloves on as time passes and bacteria emerge from the sweat and other gland orifices. In a climate like Guam, sweating of the hands, at least in most individuals, will begin very soon after scrubbing and soon will nullify the effect. The fact that some doctors break technique and contaminate gloves in putting them on is not an argument for discarding the use of gloves. Neither is the fact that poor technique in preparation of glove packs gives an unsterile product an argument for use of bare hands. Improved tactile sense without gloves is not important in minor surgery because in small incisions, one rarely inserts the finger anyway. Operation is by vision rather than by blind touch. The weight of opinion, practice, and theory would appear to be against doing even minor office surgery without gloves.

TREATMENT OF IODISM

To the Editor:—*Please give the local and systemic antidote for iodism that might occur in giving iodine by mouth or in oil for x-rays for conditions of the sinuses and chest. Is sodium chloride an antidote? If so, please give information on this and indicate recommended dosage.*

D. H. Anthony, M.D., Memphis, Tenn.

Answer.—Iodine as iodide or in organic combination is relatively innocuous and toxic reactions are not common. Specific iodine sensitivity response is best treated with maintenance of airway, intravenous fluids, "shock position," analgesics, corticoids, antihistaminics, and general care as indicated by the degree of shock, anoxia, or other acute cardiorespiratory change. Acute iodism is best treated by giving starch, flour, raw egg white, or 1% sodium thiosulfate in water by mouth, followed by emetic or lavage removal of the iodine, if the poison was taken orally. Systemic supportive measures include stimulants or anticonvulsants, opiates for pain, intravenous fluids, and corticoids. Chronic iodism is best treated by discontinuing the source of iodine. This is usually sufficient. If inflammatory signs are severe, one should also give corticoids and/or corticotropin in addition to sodium chloride, as if for chronic brominism. Suggested dosage of sodium chloride is 6 to 12 Gm. (90 to 180 grains) daily, in addition to regular dietary intake; or 1,000 cc. isotonic sodium chloride solution, intravenously or rectally, twice daily; or 1 to 2 Gm. (15 to 30 grains) sodium chloride, orally, every four hours.

RECURRENT FEVER

To the Editor:—*A 13-year-old boy has had recurrent fever for seven months. Physical examinations and complete laboratory studies, other than the sedimentation rate (Westergren), which was 24 mm. during the first hour, have all been negative for a definitive answer to the fever. A neurosurgical consultant found an abnormal electroencephalogram. Repeated spinal fluid studies showed from 60 to 80 white blood cells, mostly neutrophils, but normal hydrodynamics, serology, and protein and sugar levels in the spinal fluid. Ventriculograms revealed slight dilatation of the ventricular system, and it was noted by the neurosurgeon at the time of procedure that there was minimal cortical atrophy. Repeated cultures from the spinal fluid obtained on spinal tap and at the time of the ventriculogram grew a beta-hemolytic Streptococcus. The blood antistreptolysin titer on two occasions has been 50 and 60 Todd units. At present the boy is in a remission of his fever and feels fine.*

Two groups of questions have arisen. First, is there any relationship between the antistreptolysin titer of the blood and a streptococcic infection of the central nervous system? Is there any information available about antistreptolysin titers of the spinal fluid in the case of streptococcic infections of the central nervous system? Is there a so-called blood-brain barrier in relation to antistreptolysin titers of the blood and central nervous system infections by a Streptococcus? Second, sensitivity tests have been determined on the hemolytic Streptococcus isolated. It apparently is most sensitive to chloramphenicol and is surprisingly not sensitive to penicillin. Should we wait until this youngster has a recurrence of his fever before starting treatment; or are we more apt to sterilize the focus of infection in the central nervous system by waiting until the fever recurs; or should we start therapy at present, even though he is now afebrile and symptom free?

Horace L. Wolf, M.D., Amarillo, Texas.

Answer.—As far as is known, a streptococcic infection anywhere in the body may prompt a rise in antistreptolysin-O titer (that is, if the patient is going to form these antibodies). There do not appear to be any reports on the antistreptolysin-O titers of the spinal fluid in the case of streptococcic infection of the central nervous system. However, a rise in the antistreptolysin-O titer would be expected if the response were quantitatively significant. At the moment, it would not seem necessary to treat this child, since he is afebrile and symptom-

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free. One would question the statement that the Streptococcus is not sensitive to penicillin, since no such Streptococcus in group A has been described. If the child's problems recur, certainly a reinvestigation would be helpful.

CONSTANT SALTY TASTE IN MOUTH

To the Editor:—*A 62-year-old man complains of a constant salty taste in his mouth at the base of his tongue on the left side for the past two years. The salty taste is not present on arising but is manifest after about five minutes and is persistent throughout the day despite gargling and washing teeth. This area has been cauterized four times, and some lymphoid tissue was removed. In all instances, after healing, the salty sensation returned. The right side of the throat has normal sensations. What further in the way of diagnosis or treatment could be recommended?*

Arthur A. McAuley, M.D., Choteau, Mont.

Answer.—The only organic lesion that could possibly produce irritation and a salty taste on the posterior aspect of one side of the tongue would be some type of irritative lesion of the glossopharyngeal nerve such as a neuroma. However, there is no reason why such a lesion, if present, should produce exclusively a salty taste. It might be wise to have careful x-rays of the base of the brain in this case to be sure that there is no erosion suggestive of such a lesion. The presence of an organic lesion is questioned, and the possibility of a psychogenic disturbance as the cause of this complaint is favored.

ERGONOVINE ADMINISTRATION FOLLOWING DELIVERY

To the Editor:—*Has any hazard, untoward effect, or contraindication been found to the use of ergonovine given intravenously following delivery under low spinal (or epidural) anesthesia prior to which a vasopressor (e. g., ephedrine or Methedrine) has been administered? The question has been raised as to whether the above combination of drugs given under the stated circumstances will occasionally result in extreme degrees of hypertension. If this has been found to occur, has it been a significant finding or only an occasional one? Has there been found a definite cause-and-effect relationship? Does Pitocin, when used instead of ergonovine, cause the same effect?*

Jack B. Williams, M.D., Iowa City.

Answer.—Carvalho and others (*Am. J. Obst. & Gynec.* 65:282, 1953) called attention to the occasional rise in blood pressure following the administration of oxytocic drugs. On a large obstetric service where ergonovine is administered routinely as the baby is being delivered under saddle block, rises in blood pressure during anesthesia have been noted rarely. It is not necessary to administer a vasopressor to such patients. In cesarean section carried out with the aid of continuous spinal anesthesia and where a vasopressor drug has been administered prophylactically, a sudden and marked rise in blood pressure occurs rarely. However, the administration of 0.5 cc. of Pitocin or pituitary extract into the wall of the uterus during cesarean section quite often results in a sudden and often marked rise in blood pressure. The pharmacologists have noted no rise in blood pressure following the administration of ergonovine intravenously. Solutions of posterior pituitary extract contain varying amounts of vasopressor substances according to their purity. However, synthetic Pitocin, which has recently become available, apparently does not cause blood pressure changes.

Answer.—The use of ergonovine intravenously too soon after the administration of vasopressor such as ephedrine or d-desoxyephedrine can produce dangerous elevation in blood pressure, with cerebral hemorrhage occasionally resulting, though the occurrence is only an occasional one. An annoying rise in blood pressure has been observed more than just occasionally, perhaps in as many as 10 to 20% of patients who have received ergonovine after the injection of ephedrine. Pitocin does not produce any marked deleterious effects with respect to blood pressure or cardiac rhythm. Therefore it should be safe to use it instead of ergonovine.

CHLOASMA UTERINUM

To the Editor:—*During a first pregnancy three years ago, a woman, aged 28, first noticed a brownish pigmentation over both cheek bones and over the right eye and the upper lip. The pigmented areas did not disappear after delivery but have gradually spread over a larger area. They are always darker in the summer, but in the winter they still persist and are becoming more and more difficult to hide. The patient is a brunette and has always tanned easily in the summertime but never experienced any residual discoloration as winter came on. What can be done for the patient who has this cosmetic calamity?*

C. Campbell Stiles, M.D., East Orange, N. J.

Answer.—This woman apparently suffers from what is called chloasma uterinum. It is assumed that this woman had a thorough gynecologic examination and that no pathology was found. Symptomatic treatment of this condition usually is not very satisfactory. A harmless, sometimes helpful procedure, is the administration of vitamin C, 100 mg., three times daily, best combined with vitamin B complex. During the summertime the patient should avoid heavy exposure to the sun and should protect herself with a sun protective cream to prevent additional tanning. There are cosmetics, such as Covermark, which will satisfactorily cover up the pigmen-

tation. Surgical planing (dermabrasion) recently has been recommended and successfully used in some cases of persistent pigmentation; but such a procedure should be used only after careful consideration of all approaches, including the psychological one. The physician who posed the question speaks of a "cosmetic calamity." This would indicate that the patient is greatly, probably overly, disturbed by the pigmentation. Such a woman should receive reassurance about the harmlessness of the condition and about the fairly good prognosis; the pigmentation still may fade out in the future. If the psychological angle is too pronounced, a psychiatric consultation may be necessary.

X-RAY THERAPY FOLLOWING COLECTOMY FOR CANCER

To the Editor:—*A middle-aged woman had an adenocarcinoma, grade 2, removed from the descending colon. A large piece of colon was resected on both sides of the tumor; however, the* ***mesentery*** *contained some metastatic glands. Is there any justification for postoperative deep x-ray therapy?*

H. B. Eisenstadt, M.D., Port Arthur, Texas.

Answer.—In the experience of this consultant deep x-ray therapy postoperatively is not indicated and usually causes the patient unnecessary additional suffering.

TREATMENT OF PEDICULOSIS CAPITIS

To the Editor:—*Please outline the recent treatment for pediculosis capitis in a 5-year-old.*

M.D., Illinois.

Answer.—Pediculosis capitis responds readily to some of the newer pediculicides. One effective preparation consists of a mixture of chlorophenothane, 1.2 parts; benzyl benzoate, 15.0 parts; ethyl aminobenzoate, 2.4 parts; polysorbate 80, 3.0 parts; and bentonite magma in distilled water, 120 parts. It should be worked into the scalp and allowed to remain overnight. The head should be washed after 24 hours. One should take care to keep the emulsion away from the patient's eyes, and it should not be allowed to remain on the skin for too long a period of time. Occasionally several applications are necessary.

It is usually advisable to check for any source of reinfestation and observe routine measures of cleanliness. Combs, brushes, and hats should be thoroughly cleaned, although the organism is found primarily on the scalp. Chlorophenothane may also be employed in powder form (5% applied daily for two weeks). Benzene hexachloride, gamma, in ointment form is also effective. It should be applied at night and washed out in the morning two or three times in one week. It is usually advisable to follow these applications by scalp rinses of undiluted vinegar (for two hours) in order to loosen the eggs so that their removal may be completed by means of a fine-toothed comb or forceps. Dermatitis resulting from sensitivity to one of these newer preparations should be treated by removal of the preparation and application of soothing ointments or wet dressings.

ESTROGEN THERAPY AFTER MASTECTOMY

To the Editor:—*A patient 50 years of age had a radical breast operation four years ago, and a thorough recent physical examination has shown no recurrence. She is suffering from intense itching, day and night, with no lesions on the skin to account for it. Prior to the operation, she had similar symptoms controlled by estrogen and other female sex hormones. After the operation her surgeon told her that she must not continue with the hormones as they could be carcinogenic. Is there danger of future carcinoma caused by the use of female sex hormones during the menopause after an apparently successful operation for cancer?*

M.D., New Jersey.

Answer.—The danger of future carcinoma in women who have had female sex hormones administered during the menopause is dependent upon those unknown factors which predispose an individual to genital malignancy. There is definite evidence that estrogens will stimulate at least 50% of breast carcinomas to further growth. In spite of this, there is no justification in the generalization that the use of estrogens in women at the menopause will necessarily induce breast cancer in them. However, unrestrained, prolonged use of estrogens is to be discouraged while their judicious use can be employed. The use of estrogens in a woman after mastectomy for carcinoma is to be discouraged. Since it is assumed that 50% of breast carcinomas are estrogen dependent and also because we have no way of determining such dependency, estrogens should not be used for menopausal symptoms alone in a woman who has had a mastectomy performed for breast carcinoma.

STASIS ULCERS OF VARICOSE VEINS

To the Editor:—*What is the latest treatment, especially with topical ointments, that will assist in curing stasis ulcers of varicose veins of the leg of long duration (over 10 years)? Vascular surgery has already been performed to what is believed to be the patient's limit.*

M.D., Illinois.

Answer.— Stasis ulcers of varicose veins are usually due to chronic deep venous insufficiency with an incompetent perforator vein feeding the ulcer-

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ated area. The ulcer is usually surrounded by an induration, and the dermatitis extends above and below the induration for some distance. Usually the skin has been sensitized previously to many locally and generally administered antibiotics. Rest in bed with elevation, mild aluminum subacetate solution (1:16), and intermittent use of cortisone ointment may cool off the acute phase. When the skin lesion has been controlled by skillful dermatological care, the area may have to be excised and possibly grafted and all the incompetent perforator veins ligated above or below the fascia.

LARGE DOSES OF ASCORBIC ACID

To the Editor:—*Can there be any harm in giving large doses of ascorbic acid regularly during the winter months to a person who is susceptible to frequent colds? This person has been able to cut down colds to one or none at all a year by taking 250 mg. of ascorbic acid daily and by increasing the dose to 500 to 750 mg. for one day when he "feels a cold coming on." Can such large doses of ascorbic acid, taken practically year round, cause any imbalance of other vitamins or other essential body substances?*

Eleanor B. Townsend, M.D.,
Port Chester, N. Y.

Answer.—A daily intake of 250 mg. of ascorbic acid, with occasional increases to 750 mg., should not be harmful to a healthy individual.

PERICARDIAL HEMORRHAGE AND TREATMENT OF INFARCTION

To the Editor:—*In patients with acute myocardial infarctions with a widespread friction rub and other symptoms of pericarditis, and where the rub persists for at least 48 hours, have there been any reports that these individuals are more apt to develop bleeding into the pericardial sac or myocardial rupture if anticoagulant therapy is instituted using 100 mg. of heparin sodium subcutaneously or intravenously every eight hours, keeping clotting time below 30 minutes for 48 hours or until bishydroxycoumarin suppresses prothrombin time to therapeutic levels?*

Guerne W. de Lappe, M.D., Modesto, Calif.

Answer.—There are numerous statistically valid analyses indicating a slightly higher incidence of pericardial hemorrhage and/or myocardial rupture in patients with acute myocardial infarction treated with anticoagulants. However, in none of those that have come to this consultant's attention has there been any attempt to correlate the greater number of these complications with the presence of a friction rub, or with its duration, or with the extent of the area of its audibility. Nor can any pathological or clinical evidence be adduced to relate the auscultatory findings in question to pericardial hemorrhage, to myocardial rupture, or to the massiveness or transmurality, if you will, of the infarct. It would therefore seem that there is little or no reason for withholding anticoagulants because of the presence of a friction rub with the characteristics mentioned in the treatment of a patient with acute myocardial infarction for whom these drugs would otherwise be deemed indicated.

THE A. M. A. AND LEGISLATION

To the Editor:—*Please give information for several high school students who are studying congressional lobbying in their social science classes and have asked about the American Medical Association as a propaganda agency. M.D., California.*

Answer.—The American Medical Association is a professional organization that serves both physicians and the public. Throughout its more than 100-year history, the A. M. A. has fought to raise the quality of medical care in this country. The A. M. A. does not try to hide the fact that it promotes sound medical legislation and opposes those bills that would tend to lower standards of medical care or be incompatible with our free enterprise system. The A. M. A. is democratically organized along the lines of a federation. The individual physician in his county medical society is the key man—electing representatives to the state medical association which, in turn, elects representatives to the House of Delegates of the A. M. A. Chief policy decisions are formulated by the A. M. A.'s House of Delegates which meets twice a year. During the interim period between sessions of the House of Delegates, policy decisions are made by the Board of Trustees which meets eight or nine times a year.

Hundreds of bills pertaining to health and medicine are introduced each year to Congress—220 in the 80th Congress and 371 in the 84th Congress. The A. M. A. maintains a Washington Office to keep legislators informed on A. M. A. policies regarding various health and medical care measures and to channel information on significant legislation to members of the medical profession. In addition a Committee on Legislation, composed of physicians representing all sections of the country, studies every health and medical bill introduced in Congress.

The A. M. A. believes that it has a responsibility to the American people to take an active interest in legislation. A number of sound legislative proposals which the Association recently supported are federal aid to medical schools on a one-time construction grant basis, water-pollution-control laws,

civil-defense programming and medical stock-piling, military-career-incentive legislation, incentive-for-private-retirement programs for the self-employed, and smoke-abatement laws. The passage of a law in Congress, however, is just the first step toward putting the measure into operation. Further interpretations of the law and the final determination of practical policies fall to the governmental administrative agency concerned. The A. M. A. works with these various offices in an advisory capacity—a further indication of the medical profession's concern for the advancement of public health in America.

HYPERTENSION AND TRAUMA

To the Editor:—*In the section on Queries and Minor Notes in* The Journal, *Nov. 9, page 1357, there is an item on hypertension and trauma. It is agreed that "It is reasonable to assume that this woman had hypertension prior to the automobile accident," but it might also be well to mention that a contusion of the kidney could result in an area of infarction of the kidney. This sometimes will be the cause of hypertension and probably should be considered in the patient.*

James W. Lane, M.D.
1123 Virginia Bldg.
Charleston 1, W. Va.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Injury to the kidney, such as a contusion, is less likely to produce hypertension than is an injury resulting in renal artery thrombosis. Hypertension, for example, rarely follows surgical procedures on the kidney, including removal of stones and biopsy. Any increase in pressure that occurs usually is temporary. On the other hand, contusion as a cause of hypertension should be taken into consideration, even though the injuries of the woman in the original question apparently were so trivial that the blood pressure was not taken until three months after the accident.*

TOXICITY OF GRAPHITE

To the Editor:—*A query by Dr. Robert C. Steinman concerning the possibility of any health hazard associated with the grinding of graphite appeared in* The Journal, *Aug. 10, 1957, page 1727. In the answer to this query it is stated that there is no evidence that graphite affects the respiratory tract. Dr. Amour Liber of New York, in* The Journal, *Oct. 19, page 914, took issue with the answer. The reply to Dr. Liber is likewise open to question. In the first place, the term benign pneumoconiosis is misleading and outmoded. The deposition and accumulation of any foreign material in the bronchopulmonary tissue can hardly be considered benign. Additionally, the presence of silica in a free or combined state in graphite is the rule rather than the exception. Pneumoconiosis of graphite workers is very similar to pneumoconiosis of soft coal workers. It is a disease capable of producing clinical and laboratory changes. There are many references to substantiate these remarks.*

Louis L. Friedman, M.D.
1906 Ninth Avenue, South
Birmingham 5, Ala.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*The answerer assumed that the exposure was to the American type of graphite used in industry which is artificial graphite. The answer probably erred in not considering the natural graphite to which British workers are exposed. There is an illuminating discussion by Harding and Oliver in the* British Journal of Industrial Medicine *(6:91, 1949). The following is quoted from that journal: "Graphite or plumbago is a crystalline form of carbon which occurs in nature as soft black masses or, less commonly, as crystals in igneous rocks: this natural graphite contains varying proportions of other minerals. Graphite is also made artificially from coke, and the best preparations of this kind are nearly pure carbon. This paper will deal with some of the effects of natural graphite, and the term 'graphite' will be used to mean 'natural graphite,' that is, a mixture of minerals, largely crystalline carbon."*

Inquiry was further made of several of the large manufacturers of graphite in America. The U. S. Graphite Company responded by stating that their natural graphite is obtained from Sonora, Mexico, and contains no free silica. According to the textbook "Chemical Process Industries" (text ed. edited by Shreve, New York, McGraw–Hill Book Company, Inc., 1956), the graphite utilized in this country is artificial graphite and is 99% carbon.

It appears to this consultant that the cases of pneumoconiosis cited in the British literature are the result of the exposure to graphite containing various percentages of free silica. To the best of his knowledge such a situation does not exist in America, and this consultant was unable to find any references in the American literature on American workers suffering from a graphite pneumoconiosis, which, by the way, is sometimes referred to in the English literature as silicographitosis.